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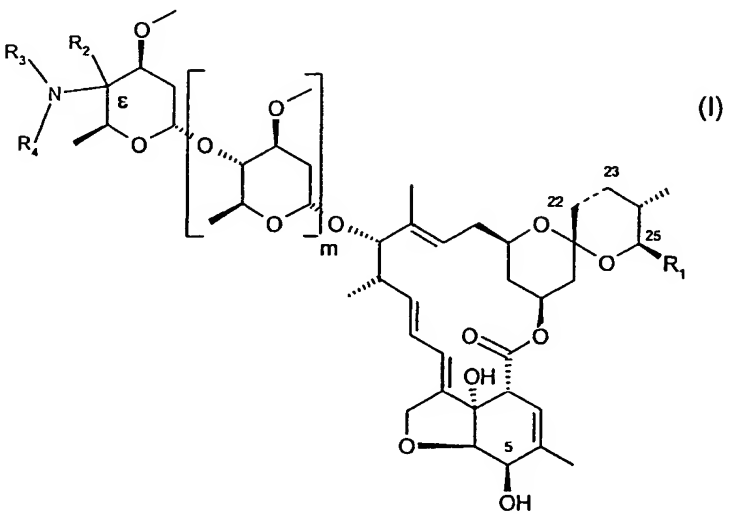
(54) Title: AVERMECTIN AND AVERMECTIN MONOSACCHARIDE SUBSTITUTED IN THE 4"- AND 4'- POSITION RESPECTIVELY



(I)

(57) Abstract: A compound of the formula (I) wherein the bond between carbon atoms 22 and 23 indicated with a broken line is a single or double bond, m is 0 or 1, R_1 represents a C_1-C_{12}alkyl, C_3-C_8cycloalkyl or C_2-C_{12}alkenyl group, R_2 represents a hydrocarbyl group or a substituted hydrocarbyl group, and R_3 and R_4 represent, independently of each other, hydrogen or a chemical constituent, or either R_2 and R_3 together or R_3 and R_4 together represent a three- to seven-membered alkylene or a four- to seven-membered alkenylene bridge, for each of which at least one, preferably a CH_2 group may be replaced by O, S or NR_6 where R_6 represents hydrogen or a hydrocarbyl group or a substituted hydrocarbyl group; or, if appropriate, an E/Z isomer and/or tautomer of the compound of formula (I), in each case in free form or in salt form.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

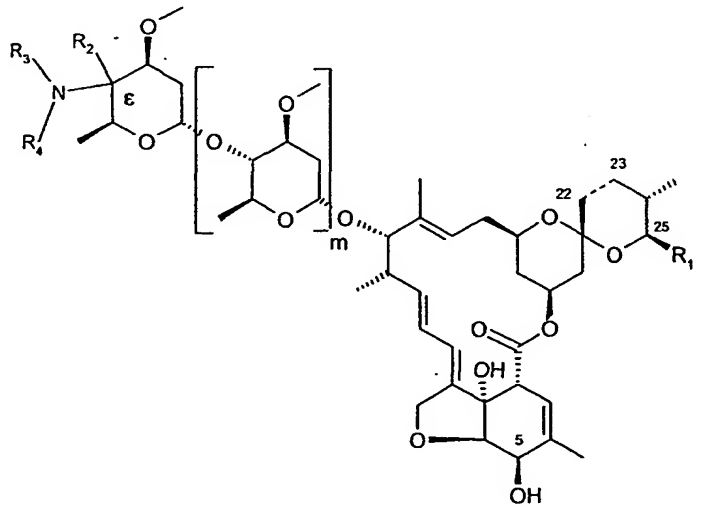
Avermectin and Avermectin monosaccharide substituted in the 4"- and 4'-position respectively

The present invention relates in particular to certain avermectin and avermectin monosaccharide derivatives, processes for preparing such derivatives, intermediates in the preparation of such derivatives, and the use of certain derivatives controlling pests.

Certain macrolide compounds for controlling pests are known. However, the biological properties of these known compounds are not entirely satisfactory, and, as a consequence, there is still a need for providing further compounds having pesticidal properties.

It is found that certain desoxy derivatives of avermectin and avermectin monosacccharide, having a hydrocarbyl group or substituted group thereof on the 4" or 4' position, are useful in controlling pests, in particular pests that are harmful to crop plants and to its propagation material, such as representatives of the class insecta, the order Acarina and the class nematoda.

Accordingly, in a first aspect, the present invention provides a compound of the formula (I)



(I),

wherein the bond between carbon atoms 22 and 23 indicated with a broken line is a single or double bond,

m is 0 or 1,

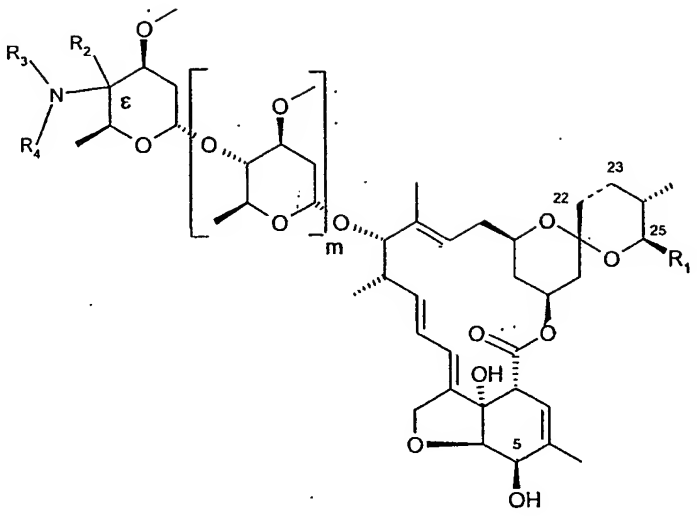
R_1 represents a C_1-C_{12}alkyl, C_3-C_8cycloalkyl or C_2-C_{12}alkenyl group,

R_2 represents a hydrocarbyl group or a substituted hydrocarbyl group, and

R_3 and R_4 represent, independently of each other, hydrogen or a chemical constituent, or either R_2 and R_3 together or R_3 and R_4 together represent a three- to seven-membered alkylene or a four- to seven-membered alkenylene bridge, for each of which at least one, preferably a CH_2 group may be replaced by O, S or NR_6, where R_6 represents hydrogen or a hydrocarbyl group or a substituted hydrocarbyl group; or, if appropriate, an E/Z isomer and/or diastereoisomer and/or tautomer of the compound of formula (I), in each case in free form or in salt form.

The symbol ε represents that the configuration of the carbon atom at the 4'- or 4"-position is *(S)* or *(R)*.

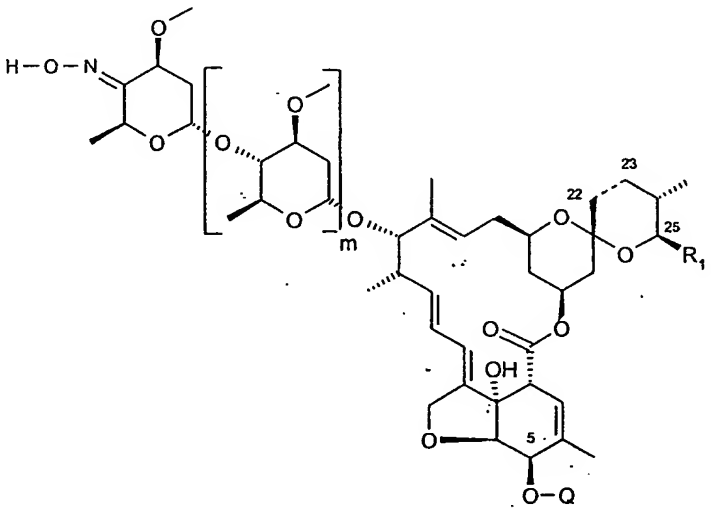
In a second aspect, the present invention provides a process for preparing a compound of formula (I)



(I)

wherein R_1, R_2, R_3, R_4, the bond between the carbon atoms 22 and 23 and m are as defined in the first aspect, comprising the steps of:

(i) synthesizing a compound of formula (α)



(α)

wherein R_1, the bond between the carbon atoms 22 and 23 and m are as defined for formula (I) in the first aspect and Q is a protecting group;

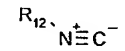
(ii) reacting a disulfide, an aliphatic or aromatic phosphine and a compound of formula (α) to yield a sulfenimine derivative of the compound of formula (α);

(iii) oxidising the sulfenimine derivative of the compound of formula (α) to yield a sulfinimine derivative of the compound of formula (α);

either

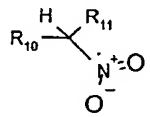
(iva) reacting an organometallic reagent having the R_2 group with the sulfinimine derivative of the compound of formula (α) to yield a desoxy – sulfinamide - hydrocarbyl derivative of the compound of formula (α); or

(ivb) reacting an isocyanate reagent of formula



where R_{12} is unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkenyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkynyl, unsubstituted or mono- to pentasubstituted aryl, unsubstituted or mono- to pentasubstituted benzyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl ester, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl ester, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl sulfone or unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl nitrile with the sulfinimine derivative of the compound of formula (α) to yield a desoxy – amine - hydrocarbyl derivative of the compound of formula (α); or

(ivc) reacting an nitro alkyl reagent of formula



where R_{10} and R_{11} are independently of each other, H, CN, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl,

unsubstituted or mono- to pentasubstituted C_2-C_{12}alkenyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkynyl, unsubstituted or mono- to pentasubstituted aryl, unsubstituted or mono- to pentasubstituted benzyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl ester, an unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl ester, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl sulfone or unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl nitrile with the sulfinimine derivative of the compound of formula (α) to yield a desoxy – amine - hydrocarbyl derivative of the compound of formula (α); and

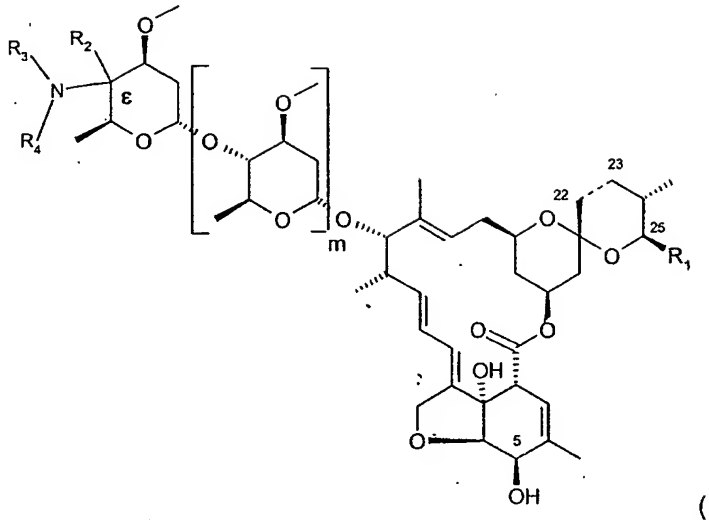
either

(va) removing the sulfinyl group and protecting group Q either in one step or sequentially one after another to yield a compound of formula (I), where R_3 and R_4 each represent hydrogen, or

(vb) removing the sulfinyl group alone, carrying out reactions on one or more of the R_2, R_3 and R_4 groups to modify the group and then removing the protecting group Q to yield a compound of formula (I), or

(vc) removing the protecting group Q if the sulfinyl group is removed during (iva) or (ivb) or (ivc) to yield a compound of formula (I).

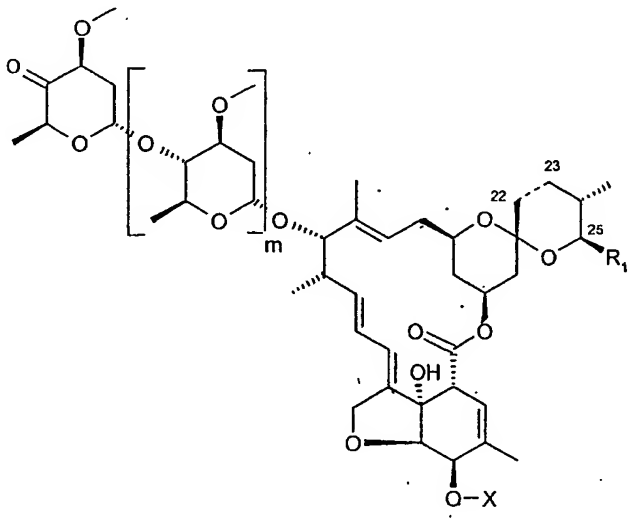
In a third aspect, the present invention provides a process for preparing a compound of formula (I)



(I)

wherein R_1, R_2, R_3, R_4, the bond between the carbon atoms 22 and 23 and m are as defined in the first aspect, comprising the steps of:

(i) synthesizing a compound of formula (β)



(β)

wherein R_1, the bond between the carbon atoms 22 and 23 and m is as defined for formula (I) in the first aspect and X is H or Q, where Q is a protecting group;

(ii) reacting N-R_4hydroxylamine or salt thereof with a compound of formula (β) to yield a nitrone derivative of the compound of formula (β);

either

(iiia) reacting an organometallic or a silyl reagent having the R_2 group with nitrone derivative of the compound of formula (β) to yield a desoxy – N-R_4hydroxylamino - hydrocarbyl derivative of the compound of formula (β), where R_4 is as defined for formula (I) of the first aspect, or

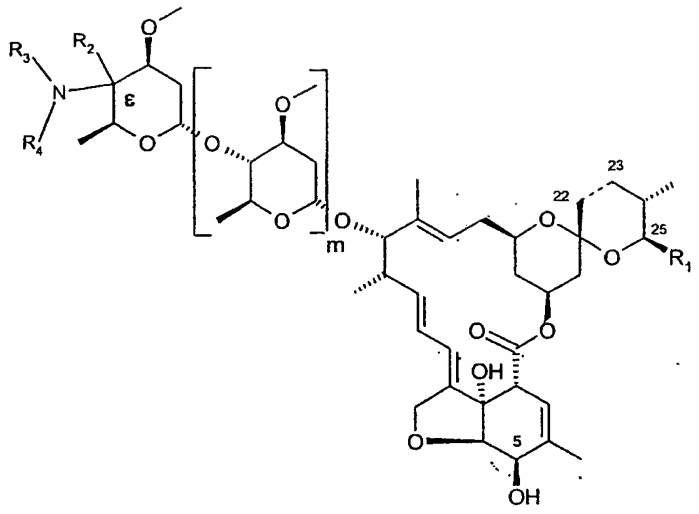
(iiib) reacting an alkene or an alkyne derivative with the nitrone derivative of the compound of formula (β) to yield a desoxy – N-isoxazolidine derivative or 2,3-dihydro-isoxazole derivative respectively of the compound of formula (β); and

either

(iva) removing the protecting group Q, if present, to yield a compound of formula (I), where R_3 is OH in the event of reaction step (iiia), or where R_2 and R_3 is an alkylene or alkenylene bridge with a CH_2 group replaced by an oxygen atom in the event of reaction step (iiib), or

(ivb) carrying out reactions on one or more of R_2, R_3 and R_4 groups to modify the group and removing the protecting group Q, if present, to yield a compound of formula (I).

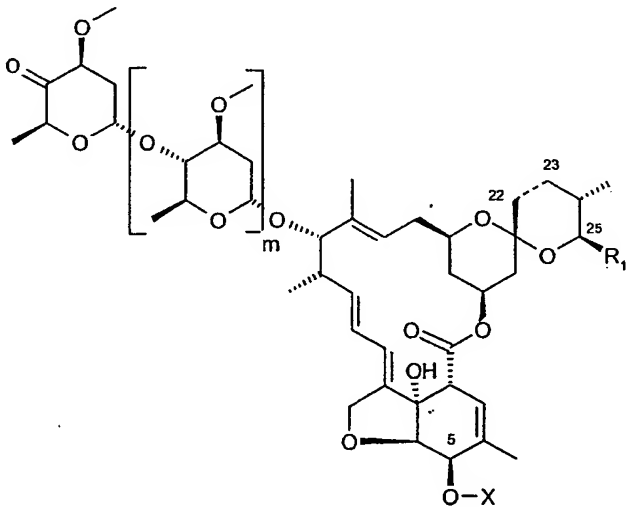
In a fourth aspect, the present invention provides a process for preparing a compound of formula (I)



(I)

wherein R_1, R_3, R_4, the bond between the carbon atoms 22 and 23 and m are as defined for formula (I) in the first aspect and R_2 is CN, comprising the steps of:

(i) synthesizing a compound of formula (β)



(β)

wherein R_1, the bond between the carbon atoms 22 and 23 and m is as defined in for formula (I) in the first aspect and X is H or Q, where Q is a protecting group;

either

(iia) reacting the compound of formula (β) with a silylated amine (having the R_3 and R_4 groups) in presence of a Lewis acid and a trialkylsilyl cyanide, to yield a compound of formula (I) with the proviso that the oxygen atom at the 5-carbon position is protected, if Q is present in the compound of formula (β), and wherein R_1, R_3, R_4, the bond between the carbon atoms 22 and 23 and m are as defined in the first aspect, and R_2 is CN, or

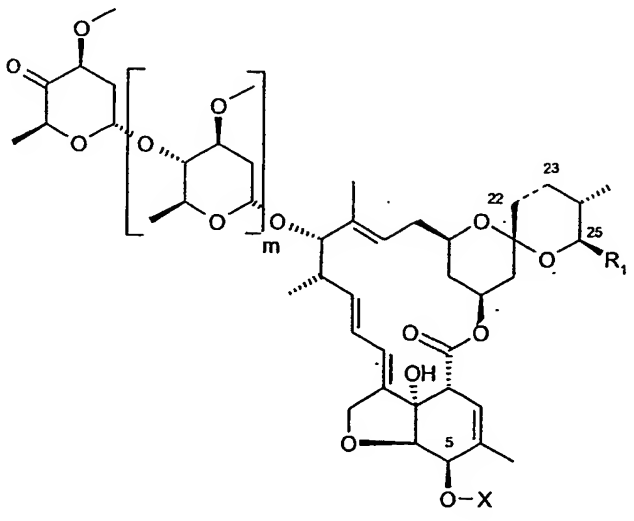
(iib) reacting the compound of formula (β) with an amine of formula R_3R_4NH, a chlorosilane, a Lewis acid and a trialkylsilyl cyanide to yield a compound of formula (I) with the proviso that the oxygen atom at the 5-carbon position is protected, if Q is present in the compound of formula (β), and wherein R_1, R_3, R_4, the bond between the carbon atoms 22 and 23 and m are as defined in the first aspect, and R_2 is CN;

(iii) optionally carrying out reactions on one or both of R_3 and R_4 groups to modify the group; and

(iv) removing the protecting group Q, if present, to yield a compound of formula (I);

or

(i) synthesizing a compound of formula (β)



(β)

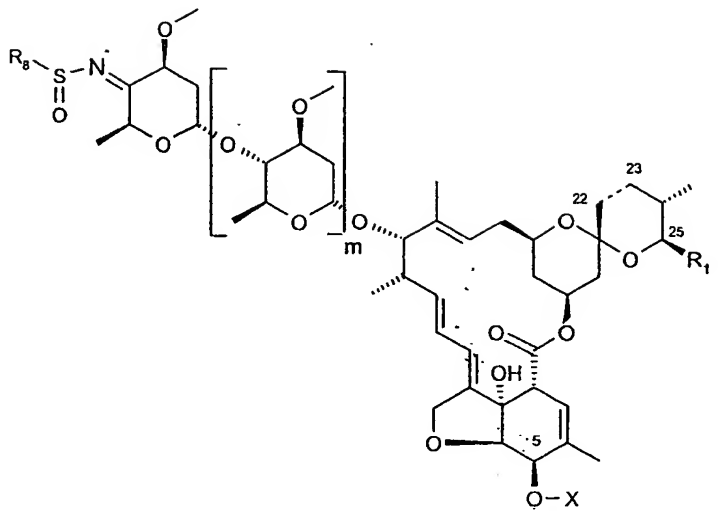
wherein R_1, the bond between the carbon atoms 22 and 23 and m are as defined for formula (I) in the first aspect and X is H or Q, where Q is a protecting group;

(ii) reacting the compound of formula (β) with an ammonium salt of formula $R_{18}CO_2^-NH_4^+$, an isocyanide of formula $R_{12}NC$ to yield a compound of formula (I), with the proviso that the oxygen atom at the 5-carbon position is protected, if Q is present in the compound of formula (β), wherein R_1, the bond between the carbon atoms 22 and 23 and m are as defined in the first aspect, R_2 is $R_{12}NHC(O)$, and R_4 is $R_{18}C(O)$, R_{18} is H, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkenyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkynyl, unsubstituted or mono- to pentasubstituted aryl, unsubstituted or mono- to pentasubstituted benzyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl ester, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl ester, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl sulfone or unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl nitrile and R_{12} is as defined in (ivb) of the second aspect; and

(iii) removing the protecting group Q, if present, to yield a compound of formula (I).

Generally, a preparation of a compound of formula (I) results in a mixture of compounds, so the present invention also extends to a mixture containing compounds of formula (I), such as a mixture containing E and Z isomers, *R* and *S* diastereoisomers, compounds with R_1 is iPr and compounds with R_1 is *sec*-Bu or compounds of different tautomers, or a mixture thereof.

In a fifth aspect, the present invention provides a compound of the formula (III)



(III)

wherein the bond between carbon atoms 22 and 23 indicated with a broken line is a single or double bond;

m is 0 or 1;

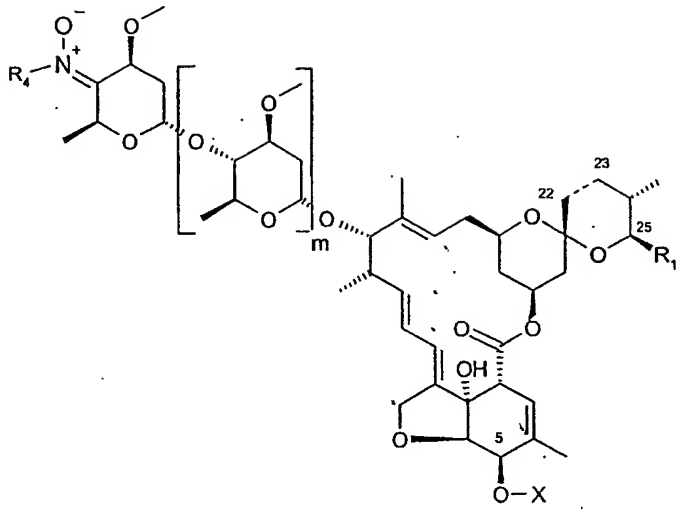
R_1 represents a C_1-C_{12}alkyl, C_3-C_8cycloalkyl or C_2-C_{12}alkenyl, group;

R_8 represents C_1-C_6alkyl that is optionally substituted with one to five substituents selected from the group consisting of halogen, C_1-C_6alkoxy, hydroxy, cyano, aryl, benzyl or heteroaryl, which, depending on the possibilities of substitution on the ring, are mono- to trisubstituted by substituents selected from the group consisting of OH, halogen, CN, NO_2, C_1-C_{12}alkyl, C_1-C_{12}haloalkyl, C_1-C_{12}alkoxy, C_1-C_{12}haloalkoxy, C_1-C_{12}alkylthio and C_1-C_{12}haloalkylthio, and

X represents H or Q, where Q is a suitable protecting group to prevent reaction on the oxygen atom at the 5-carbon position.

or, if appropriate, an E/Z isomer and/or diastereoisomer and/or tautomer of the compound of formula (III), in each case in free form or in salt form.

In a sixth aspect, the present invention provides a compound of the formula (V)



(V)

wherein the bond between carbon atoms 22 and 23 indicated with a broken line is a single or double bond,

m is 0 or 1,

R_1 represents a C_1-C_{12}alkyl, C_3-C_8cycloalkyl or C_2-C_{12}alkenyl, group,

R_4 represents a chemical constituent, and

X represents H or Q, where Q is a suitable protecting group to prevent reaction on the oxygen atom at the 5-carbon position; or, if appropriate, an E/Z isomer and/or diastereoisomer and/or tautomer of the compound of formula (V), in each case in free form or in salt form.

In a seventh aspect, the present invention provides a pesticidal composition comprising at least one compound of the formula (I), (III) or (V), as defined in the first, fifth or sixth aspect respectively, as active compound, and at least one auxiliary.

In an eighth aspect, the present invention provides a method for controlling pests comprising applying a composition defined in the seventh aspect to the pests or their habitat.

In a ninth aspect, the present invention provides a process for preparing a composition defined in the seventh aspect comprising mixing intimately and/ or grinding at least one compound of the formula (I), (III) or (V), as defined in the first, fifth or sixth aspect respectively, as active compound, with at least one auxiliary.

In a tenth aspect, the present invention provides the use of a compound of the formula (I), (III) or (V), as defined in the first, fifth or sixth aspect respectively, for preparing a composition as defined in the seventh aspect.

In an eleventh aspect, the present invention provides the use of a composition as defined in the seventh aspect for controlling pests.

In a twelfth aspect, the present invention provides a method for protecting plant propagation material comprising treating the propagation material, or the location where the propagation material is planted, with a composition defined in the seventh aspect.

In a thirteenth aspect, the present invention provides a pest resistant plant propagation material having adhered thereto at least one compound of the formula (I), (III) or (V), as defined in the first, fifth or sixth aspect respectively; preferably treated by the method of the twelfth aspect.

In a fourteenth aspect, the present invention provides the use of compound defined in the fifth or sixth aspect for preparing a compound of formula (I) as defined in the first aspect.

A compound of the present invention is a derivative of avermectin or avermectin monosaccharide.

Avermectins are known to the person skilled in the art. They are a group of structurally closely related pesticidally active compounds, which are obtained by fermenting a strain of the microorganism Streptomyces avermitilis. Also the derivatives where R_1 is not iso-propyl or sec-butyl, for example, it is cyclohexyl or 1-methyl butyl, are obtained by fermentation. Derivatives of Avermectins can be obtained by conventional chemical syntheses. The present invention relates to a new series of compounds having a hydrocarblyl group or substituted group thereof and an unsubstituted or substituted amine on the 4" or 4' position of avermectin or avermectin monosaccharide respectively.

The avermectins, which can be obtained from Streptomyces avermitilis, are referred to as A1a, A1b, A2a, A2b, B1a, B1b, B2a and B2b. The compounds referred to as "A" and "B" have a methoxy radical and an OH group, respectively, in the 5-position. The "a" series and the "b" series are compounds in which the substituent R_1 (in position 25) is a sec-butyl radical and an isopropyl radical, respectively. The number 1 in the name of the compounds means that carbon atoms 22 and 23 are linked by a double bond; the number 2 means that they are linked by a single bond and that the carbon atom 23 carries an OH group. The above nomenclature is adhered to in the description of the present invention to denote the specific structure type in the not naturally occurring avermectin derivatives according to the invention, which corresponds to the naturally occurring avermectin. The compounds according to the invention are especially derivatives of avermectin compounds of the B1 series, advantageously B1a and B1b; derivatives having a single bond between carbon atoms 22 and 23; derivatives having substituents other than sec-butyl or isopropyl in position 25; and derivatives of the corresponding monosaccharides.

For a review of macrolide chemistries, see: Ivermectin and Abamectin. Fisher, M. H.; Mrozik, H. Editor(s) - Campbell, William Cecil, (1989), 1-23; and Macrolide Antibiotics (2nd Edition), Sunazuka, Toshiaki, Omura, Sadafumi; Iwasaki, Shigeo, Omura, Satoshi. Editor(s) - Omura, Satoshi (2002), 99-180.

Also the following articles describe synthetic routes to prepare monosaccharide avermectin derivatives: Mrozik, Helmut; Eskola, Philip; Arison, Byron H.; Albers-Schoenberg, George;

Fisher, Michael H. Journal of Organic Chemistry (1982), 47(3), 489-92; and Bliard, Christophe; Escribano, Francisca Cabrera; Lukacs, Gabor; Olesker, Alain; Sarda, Pierre Journal of the Chemical Society, Chemical Communications (1987), 5), 368-70.

EP-A-0343708 further describes synthetic routes to prepare 4" or 4'-oxo and oxime avermectin derivatives.

Each compound of the invention may be present as a tautomer. Accordingly, the compound, for example, of formula (I) is, if appropriate, also to be understood as including the corresponding tautomer, even if the latter are not specifically mentioned in each case.

Each compound of the invention, such as compound of formula (I), and, where applicable, its tautomer can form salts, for example acid addition salts. These acid addition salts are formed, for example, with strong inorganic acids, such as mineral acids, for example, sulfuric acid, a phosphoric acid or a hydrohalic acid, with strong organic carboxylic acids, such as unsubstituted or substituted, for example halo-substituted, C_1-C_4alkanecarboxylic acids, for example, acetic acid, unsaturated or saturated dicarboxylic acids, for example, oxalic acid, malonic acid, maleic acid, fumaric acid or phthalic acid, hydroxycarboxylic acids, for example, ascorbic acid, lactic acid, malic acid, tartaric acid or citric acid, or benzoic acid, or with organic sulfonic acids, such as unsubstituted or substituted, for example, halo-substituted, C_1-C_4alkane- or aryl-sulfonic acids, for example, methane- or p-toluene-sulfonic acid. Compound of formula (I) that have at least one acidic group can furthermore form salts with bases. Suitable salts with bases are, for example, metal salts, such as alkali metal salts or alkaline earth metal salts, for example, sodium, potassium or magnesium salts, or salts with ammonia or with an organic amine, such as morpholine, piperidine, pyrrolidine, a mono-, di- or tri-lower alkylamine, for example, ethylamine, diethylamine, triethylamine or dimethylpropylamine, or a mono-, di- or trihydroxy-lower alkylamine, for example, mono-, di- or tri-ethanolamine. Corresponding internal salts may also be formed where appropriate. Among the salts of the compound of formula (I), the agrochemically advantageous salts are preferred.

Any reference to the free compound of the invention, for example, of formula (I) or its salt, is to be understood as including, where appropriate, also the corresponding salt or the free compound of formula (I), respectively. The same applies to tautomer of compound of the invention, for example, of formula (I) and salt thereof.

The invention is described in detail below. Further, as described below each embodiment of a feature of the present invention is independent of an embodiment of another feature.

In the context of the first aspect of the invention, preference is given to following groups:

(2) a compound of the first aspect (also referred to as group (1)) in free form (*i.e.*, not in salt form);

(3) a compound of the first aspect (also referred to as group (1)) in salt form;

(4) a compound according to any one of groups (1) to (3), wherein R_2 is unsubstituted C_1-C_{12}alkyl or halogen-substituted C_1-C_{12}alkyl or in each case a mono- to pentasubstituted derivative thereof, unsubstituted C_3-C_8cycloalkyl or halogen-substituted C_3-C_8cycloalkyl or in each case a mono- to pentasubstituted derivative thereof, unsubstituted C_2-C_{12}alkenyl or halogen-substituted C_2-C_{12}alkenyl or in each case a mono- to pentasubstituted derivative thereof, unsubstituted C_2-C_8alkynyl or halogen-substituted C_2-C_8alkynyl or in each case a mono- to pentasubstituted derivative thereof, CN, unsubstituted aryl or heterocyclyl, or aryl or heterocyclyl that are, depending on the possibilities of substitution on the ring, mono- to pentasubstituted by substituents selected from the group consisting of =O, OH, =S, SH, halogen, CN, NO_2, C_1-C_{12}alkyl, C_3-C_8cycloalkyl, C_1-C_{12}haloalkyl, C_1-C_{12}alkoxy, C_1-C_{12}haloalkoxy, C_1-C_{12}alkylthio, C_1-C_{12}haloalkylthio, C_1-C_6alkoxy-C_1-C_6alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, phenoxy and methylenedioxy;

(5) a compound according to any one of groups (1) to (4), wherein R_3 is hydrogen, unsubstituted C_1-C_{12}alkyl or halogen-substituted C_1-C_{12}alkyl or in each case a mono- to

pentasubstituted derivative thereof, unsubstituted C_3-C_8cycloalkyl or halogen-substituted C_3-C_8cycloalkyl or in each case a mono- to pentasubstituted derivative thereof, unsubstituted C_2-C_{12}alkenyl or halogen-substituted C_2-C_{12}alkenyl or in each case a mono- to pentasubstituted derivative thereof, unsubstituted C_2-C_8alkynyl or halogen-substituted C_2-C_8alkynyl or in each case a mono- to pentasubstituted derivative thereof, unsubstituted C_1-C_{12}alkoxy or halogen-substituted C_1-C_{12}alkoxy or in each case a mono- to pentasubstituted derivative thereof, unsubstituted or mono- to pentasubstituted phenoxy, OH, aryl, benzyl, heterocyclyl group, CN, $-N(R_5)_2$, $-SR_8$, $-S(=O)R_8$, $-S(=O)_2R_8$, or $-S(=O)_2N(R_5)_2$;

(6) a compound according to any one of groups (1) to (5), wherein R_4 is H, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkenyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkynyl;

(7) a compound according to any one of groups (1), (2), (3) and (6), wherein R_2 and R_3 together are a three- to seven-membered alkylene or a four- to seven-membered alkenylene bridge, for each of which at least one, preferably a, CH_2 group may be replaced by O, S or NR_6;

(8) a compound according to any one of groups (1) to (4), wherein R_3 and R_4 together are a three- to seven-membered alkylene or a four- to seven-membered alkenylene bridge, for each of which at least one, preferably a, CH_2 group may be replaced by O, S or NR_6;

The substituents of the alkyl, alkoxy, phenoxy, alkenyl, alkynyl, alkylene (whether CH_2 group replaced or not), alkenylene (whether CH_2 group replaced or not), cycloalkyl groups, and halogen substituted groups of alkyl, alkenyl, alkynyl and cycloalkyl, mentioned in any one of groups (1) to (8) are selected from the group consisting of OH, SH, =O, =S, halogen, CN, SCN, NO_2, $-N_3$, C_3-C_8-cycloalkyl that is unsubstituted or substituted by one to three methyl groups, C_3-C_8cycloalkenyl that is unsubstituted or substituted by one to three methyl

groups, C_3-C_8halocycloalkyl, C_1-C_{12}alkoxy, halo-C_1-C_{12}alkoxy, C_2-C_8alkenyloxy, C_2-C_8alkynyloxy, C_1-C_6alkoxy-C_1-C_6alkoxy, C_1-C_{12}alkoxy-$N(R_5)_2$ (wherein the two R_5 are independently of each other), C_3-C_8cycloalkoxy, C_1-C_{12}alkylthio, C_1-C_6alkylthio-C_1-C_6alkoxy, halo-C_1-C_{12}alkylthio, C_3-C_8cycloalkylthio, C_3-C_8heterocycloalkylthio, C_1-C_{12}alkylsulfinyl, C_3-C_8cycloalkylsulfinyl, C_1-C_{12}haloalkylsulfinyl, C_3-C_8halocycloalkylsulfinyl, C_1-C_{12}alkylsulfonyl, C_3-C_8cycloalkylsulfonyl, C_1-C_{12}haloalkylsulfonyl, C_3-C_8halocycloalkylsulfonyl, $-N(R_5)_2$ (wherein the two R_5 are independently of each other or the two R_5 together represent a three- to seven-membered alkylene or a four- to seven-membered alkenylene bridge), $-C(=Y)OH$, $-C(=Y)R_7$, $-X-C(=Y)R_7$, $-P(=O)(OC_1$-$C_6alkyl)_2$, $-S(=O)_2R_8$, $-NH-S(=O)_2R_8$, $-X-C(=O)-C_1$-C_6alkyl-$S(=O)_2R_8$, aryl, benzyl, heterocyclyl, aryloxy, benzyloxy, heterocyclyloxy, arylthio, benzylthio, heterocyclylthio, and aryl, benzyl, heterocyclyl, aryloxy, benzyloxy, heterocyclyloxy, arylthio, benzylthio and heterocyclylthio, which, depending on the possibilities of substitution on the ring, are mono- to pentasubstituted by substituents selected from the group consisting of =O, OH, =S, SH, halogen, CN, NO_2, C_1-C_{12}alkyl, C_3-C_8cycloalkyl, C_1-C_{12}haloalkyl, C_1-C_{12}alkoxy, C_1-C_{12}haloalkoxy, C_1-C_{12}alkylthio, C_1-C_{12}haloalkylthio, C_1-C_6alkoxy-C_1-C_6alkyl, dimethylamino-C_1-C_6alkoxy, C_2-C_8alkenyl, C_2-C_8alkynyl, phenoxy, phenyl-C_1-C_6alkyl, methylenedioxy, $-N(R_5)_2$ (wherein the two R_5 are independently of each other), $-O-C(=O)-R_7$, $-NH-C(=O)R_7$, $-C(=O)R_9$, C_1-C_6alkylsulfinyl, C_3-C_8cycloalkylsulfinyl, C_1-C_6haloalkylsulfinyl, C_3-C_8halocycloalkylsulfinyl, C_1-C_6alkylsulfonyl, C_3-C_8cycloalkylsulfonyl, C_1-C_6haloalkylsulfonyl and C_3-C_8halocycloalkylsulfonyl;

where

R_5 represents H, C_1-C_6alkyl that is optionally substituted with one to five substituents selected from the group consisting of halogen, C_3-C_8-cycloalkoxy, hydroxy and cyano, C_1-C_6alkoxy, C_3-C_8-cycloalkyl, C_2-C_{12}alkenyl, C_2-C_8alkynyl, aryl, benzyl, heteroaryl, or aryl, benzyl or heteroaryl, which, depending on the possibilities of substitution on the ring, are mono- to trisubstituted by substituents selected from the group consisting of OH, halogen, CN, NO_2, C_1-C_{12}alkyl, C_1-C_{12}haloalkyl, C_1-C_{12}alkoxy, C_1-C_{12}haloalkoxy, C_1-C_{12}alkylthio and C_1-C_{12}haloalkylthio;

R_6 represents H, C_1-C_8alkyl, hydroxy-C_1-C_8alkyl, C_3-C_8cycloalkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, phenyl, benzyl, -C(=O)R_9 or -CH_2-C(=O)R_9;

R_7 represents H, C_1-C_{24}alkyl, C_1-C_{12}haloalkyl, C_1-C_{12}hydroxyalkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, C_1-C_{12}alkoxy, C_1-C_6alkoxy-C_1-C_6alkoxy, C_2-C_8alkenyloxy, C_1-C_6alkoxy-C_1-C_6alkyl, $N(R_5)_2$ (wherein the two R_5 are independently of each other), aryl, benzyl, heterocyclyl, or aryl, benzyl or heterocyclyl, which, depending on the possibilities of substitution on the ring, are mono- to trisubstituted by substituents selected from the group consisting of OH, halogen, CN, NO_2, C_1-C_{12}alkyl, C_1-C_{12}haloalkyl, C_1-C_{12}alkoxy, C_1-C_{12}haloalkoxy, C_1-C_{12}alkylthio and C_1-C_{12}haloalkylthio;

R_8 represents C_1-C_6alkyl that is optionally substituted with one to five substituents selected from the group consisting of halogen, C_1-C_6alkoxy, hydroxy, cyano and benzyl, aryl, benzyl, heteroaryl, or aryl, benzyl or heteroaryl, which, depending on the possibilities of substitution on the ring, are mono- to trisubstituted by substituents selected from the group consisting of OH, halogen, CN, NO_2, C_1-C_{12}alkyl, C_1-C_{12}haloalkyl, C_1-C_{12}alkoxy, C_1-C_{12}haloalkoxy, C_1-C_{12}alkylthio and C_1-C_{12}haloalkylthio;

R_9 represents H, OH, SH, -$N(R_5)_2$ (wherein the two R_5 are independently of each other), C_1-C_{24}alkyl, C_2-C_{12}alkenyl, C_1-C_8hydroxyalkyl, C_1-C_{12}haloalkyl, C_1-C_{12}alkoxy, C_1-C_{12}haloalkoxy, C_1-C_6alkoxy-C_1-C_6alkyl, C_1-C_6alkoxy-C_1-C_6alkoxy, C_1-C_6alkoxy-C_1-C_6alkoxy-C_1-C_6alkyl, C_1-C_{12}alkylthio, C_2-C_8alkenyloxy, C_2-C_8alkynyloxy, -X-C_1-C_6alkyl-C(=O)R_7, -C_1-C_6alkyl-S(=O)$_2R_8$, aryl, benzyl, heterocyclyl, aryloxy, benzyloxy, heterocyclyloxy, or aryl, benzyl, heterocyclyl, aryloxy, benzyloxy or heterocyclyloxy, which, depending on the possibilities of substitution on the ring, are mono- to trisubstituted in the ring independently of one another by halogen, NO_2, C_1-C_6alkyl, C_1-C_6alkoxy, C_1-C_6haloalkyl or C_1-C_6haloalkoxy;

X represents O, S, NH or N-C_1-C_6alkyl; and

Y represents O or S.

Furthermore, preference is given to

(9) a compound according to any one of groups (1) to (8), wherein R_1 is isopropyl, or sec-butyl;

(10) a compound according to any one of groups (1) to (8), wherein R_1 is cyclohexyl;

(11) a compound according to any one of groups (1) to (8), wherein R_1 is 1-methyl-butyl;

(12) a compound according to any one of groups (1) to (11), wherein the bond between carbon atoms 22 and 23 is a single bond;

(13) a compound according to any one of groups (1) to (11), wherein the bond between carbon atoms 22 and 23 is a double bond;

(14) a compound according to any one of groups (1) to (13), wherein m is 1;

(15) a compound according to any one of groups (1) to (13), wherein m is 0;

(16) a compound according to any one of groups (1) to (15), wherein the configuration of the carbon atom at the ε-position is (*S*);

(17) a compound according to any one of groups (1) to (15), wherein the configuration of the carbon atom at the ε-position is (*R*);

(18) a compound according to any one of groups (1) to (6) and (8) to (17), wherein R_2 is -CH_3, -$CH{=}CH_2$, -$C{\equiv}N$, $H_2C{=}CH{-}CH_2$-, -$C{\equiv}CH$ or $(CH_3)_2CHNHC(O)$;

(19) a compound according to any one of groups (1) to (6) and (9) to (18), wherein R_3 is H, -CH_3, -$C(O)CH_3$, -$C(O)CH_2CH_3$, -$C(O)CH_2CH_2CH_3$, -$C(O)CH_2OCH_3$, -$C(O)CH_2OCH_2CH_3$, -$C(O)OCH_3$ or -C(O)H;

(20) a compound according to any one of groups (1) to (7) and (9) to (19), wherein R_4 is either H or -CH_3;

(21) a compound according to any one of groups (1) to (3), (6), (7), (9) to (17), and (20), wherein R_2 and R_3 together either represent -$CH_2CH_2CH{=}CHCH_2$- or –$CH_2CH{=}CHCH_2$-; or

(22) a compound according to any one of groups (1) to (4) and (8) to (18), wherein R_3 and R_4 together either represent -$CH_2CH_2CH{=}CHCH_2$- or –$CH_2CH{=}CHCH_2$-.

A preferred compound of formula (I) is where R_1 is isopropyl or sec-butyl, m is 1, the stereochemistry at the ε-position is (*S*), R_2 is a group containing 1 to 3 carbon atoms, R_3 is hydrogen or a group containing 1 to 4 carbon atoms and one or two oxygen atoms and R_4 is hydrogen or a group containing 1 to 3 carbon atoms.

Where the same general group (or radical or substituent) type is described as present in a compound in two or more positions, the specific groups may be the same or different. Further, where a number range of substitution is indicated, for example, mono- to pentasubstituted C_1 to C_{12}alkyl, a skilled person would understand that extent of substitutions would depend on the availability of substitution sites. Unless defined otherwise, the general terms used in the present application have the meanings given below:

Chemical constituent, preferably an organic group, is a group of atoms attached *via* an atom selected from carbon, nitrogen, sulfur, oxygen, or phosphorus. Preferably the attaching atom is carbon, nitrogen, sulfur or oxygen. Examples include unsubstituted and substituted hydrocarbyl groups, carbonate and derivatives, nitrate and derivatives, phosphate and derivatives, sulfate and derivatives, OH, amine and derivatives, alkoxy groups, thio groups, sulfinyl groups and sulfonyl groups.

Hydrocarbyl group is a group of atoms attached *via* a carbon atom. The group contains one or more carbon atoms and one or more hydrogen atoms, which group can be aliphatic, alicyclic, (each saturated or unsaturated), aromatic, straight-chained, branched-chained, or a group with a combination thereof. Examples include methyl, ethyl, isopropyl, cyclohexyl, vinyl, ethynyl, allyl, phenyl, or benzyl. Preferably a hydrocarbyl group contains 1 to 15, more preferably 1 to 12, especially 1 to 4, such as 1 or 2, carbon atoms.

Substituted hydrocarbyl group is a group of atoms attached *via* a carbon atom. The group contains one or more carbon atoms, optionally one or more hydrogen atoms, and one or more hetero atoms, such as a halogen, boron, oxygen, nitrogen, sulfur, phosphorus, or a mixture thereof. Examples include cyano, halogen substituted carbon-containing groups, alkoxy groups, heterocyclic groups, such as pyridine and derivatives thereof, and carbonyl containing groups. Preferably a substituted hydrocarbyl group contains 1 to 15, more preferably 1 to 12, especially 1 to 4, such as 1 to 2, carbon atoms.

Unless defined otherwise, carbon-containing groups (for example, alkyl, alkenyl, cycloalkyl) contain 1 up to and including 6, preferably 1 up to and including 4, in particular 1 or 2, carbon atoms.

Halogen - as a group per se and also as a structural element of other groups and compounds, such as haloalkyl, haloalkoxy and haloalkylthio - is fluorine, chlorine, bromine or iodine, in particular fluorine, chlorine or bromine, especially fluorine or chlorine.

Alkyl - as a group per se and also as a structural element of other groups and compounds, such as haloalkyl, alkoxy and alkylthio - is, in each case taking into account the number of carbon atoms contained in each case in the group or compound in question, either straight-chain, *i.e.*, methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl or octyl, or branched, for example, isopropyl, isobutyl, sec-butyl, tert-butyl, isopentyl, neopentyl or isohexyl. Preferred number of carbon atoms in an alkyl group is between 1 to 6, such as 1 to 4.

Cycloalkyl - as a group per se and also as a structural element of other groups and compounds, such as, for example, of halocycloalkyl, cycloalkoxy and cycloalkylthio - is, in each case taking into account the number of carbon atoms contained in each case in the group or compound in question, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl or cyclooctyl. Preferred number of carbon atoms in a cycloalkyl group is between 3 to 6, such as 3 to 4.

Alkenyl - as a group per se and also as a structural element of other groups and compounds - is, taking into account the number of carbon atoms and conjugated or isolated double bonds contained in the group, either straight-chain, for example, vinyl, allyl, 2-butenyl, 3-pentenyl, 1-hexenyl, 1-heptenyl, 1,3-hexadienyl or 1,3-octadienyl, or branched, for example, isopropenyl, isobutenyl, isoprenyl, tert-pentenyl, isohexenyl, isoheptenyl or

isooctenyl. Preference is given to alkenyl groups having 3 to 12, in particular 3 to 6, especially 3 or 4, carbon atoms.

Alkynyl – as a group per se and also as a structural element of other groups and compounds - is, in each case taking into account the number of carbon atoms and conjugated or isolated double bonds contained in the group or compound in question, either straight-chain, for example, ethynyl, propargyl, 2-butynyl, 3-pentynyl, 1-hexynyl, 1-heptynyl, 3-hexen-1-ynyl or 1,5-heptadien-3-ynyl, or branched, for example, 3-methylbut-1-ynyl, 4-ethylpent-1-ynyl, 4-methylhex-2-ynyl or 2-methylhept-3-ynyl. Preference is given to alkynyl groups having 3 to 12, in particular 3 to 6, especially 3 or 4, carbon atoms.

Alkoxy - as a group per se and also as a structural element of other groups and compounds is, in each case taking into account the number of carbon atoms contained in each case in the group or compound in question, either straight-chain, *e.g.*, methoxy, ethoxy or propoxy, or branched-chain, for example, isopropoxy, isobutyoxy, or sec-butoxy. One or more oxygen atoms can be present in the group. Preferred number of carbon atoms in an alkoxy group is between 1 to 6, such as 1 to 4. Similarly, the oxygen atom in the group alkenyloxy or alkynyloxy can be in any position and the preferred number of carbon atoms in either group is between 2 to 6, such as 2 to 4.

Halogen-substituted carbon-containing groups and compounds, such as, for example, halogen-substituted alkyl, alkenyl, alkynyl, cycloalkyl, alkoxy or alkylthio, can be partially halogenated or perhalogenated, where in the case of polyhalogenation the halogen substituents can be identical or different. Examples of haloalkyl - as a group per se and also as a structural element of other groups and compounds, such as haloalkoxy or haloalkylthio - are methyl which is mono- to trisubstituted by fluorine, chlorine and/or bromine, such as CHF_2 or CF_3; ethyl which is mono- to pentasubstituted by fluorine, chlorine and/or bromine, such as CH_2CF_3, CF_2CF_3, CF_2CCl_3, CF_2CHCl_2, CF_2CHF_2, CF_2CFCl_2, CF_2CHBr_2, CF_2CHClF, CF_2CHBrF or $CClFCHClF$; propyl or isopropyl which is mono- to heptasubstituted by fluorine, chlorine and/or bromine, such as $CH_2CHBrCH_2Br$, CF_2CHFCF_3, $CH_2CF_2CF_3$, $CF(CF_3)_2$ or $CH(CF_3)_2$; butyl or one of its isomers, mono- to

nonasubstituted by fluorine, chlorine and/or bromine, such as $CF(CF_3)CHFCF_3$ or $CH_2(CF_2)_2CF_3$; pentyl or one of its isomers, mono- to undecasubstituted by fluorine, chlorine and/or bromine, such as $CF(CF_3)(CHF_2)CF_3$ or $CH_2(CF_2)_3CF_3$; and hexyl or one of its isomers, mono- to tridecasubstituted by fluorine, chlorine and/or bromine, such as $(CH_2)_4CHBrCH_2Br$, $CF_2(CHF)_4CF_3$, $CH_2(CF_2)_4CF_3$ or $C(CF_3)_2(CHF)_2CF_3$.

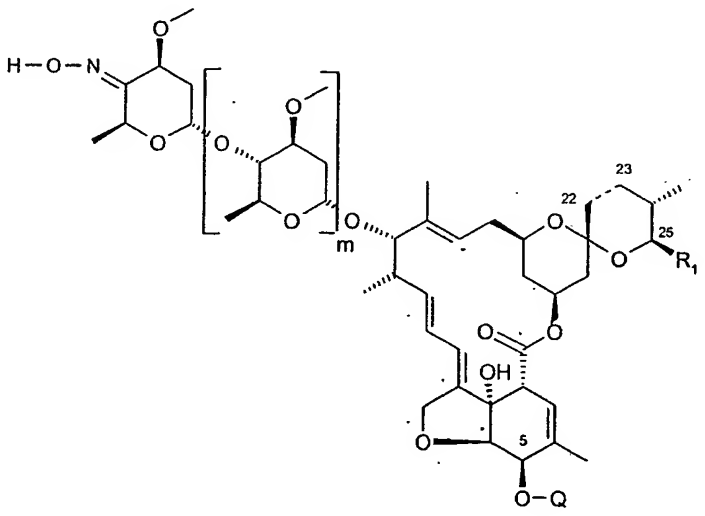
Aryl is in particular phenyl, naphthyl, anthracenyl, phenanthrenyl, perylenyl or fluorenyl, preferably phenyl.

Heterocyclyl is understood as being a three- to seven-membered monocyclic ring, which may be saturated or unsaturated, and that contains from one to three hetero atoms selected from the group consisting of B, N, O and S, especially N and S; or a bicyclic ring system having from 8 to 14 ring atoms, which may be saturated or unsaturated, and that may contain either in only one ring or in both rings independently of one another, one or two hetero atoms selected from N, O and S; heterocyclyl is in particular piperidinyl, piperazinyl, oxiranyl, morpholinyl, thiomorpholinyl, pyridyl, N-oxidopyridinio, pyrimidyl, pyrazinyl, s-triazinyl, 1,2,4-triazinyl, thienyl, furanyl, dihydrofuranyl, tetrahydrofuranyl, pyranyl, tetrahydropyranyl, pyrrolyl, pyrrolinyl, pyrrolidinyl, pyrazolyl, imidazolyl, imidazolinyl, thiazolyl, isothiazolyl, triazolyl, oxazolyl, thiadiazolyl, thiazolinyl, thiazolidinyl, oxadiazolyl, dioxaborolanyl, phthalimidoyl, benzothienyl, quinolinyl, quinoxalinyl, benzofuranyl, benzimidazolyl, benzpyrrolyl, benzthiazolyl, indolinyl, isoindolinyl, cumarinyl, indazolyl, benzothiophenyl, benzofuranyl, pteridinyl or purinyl, which are preferably attached via a C atom; thienyl, benzofuranyl, benzothiazolyl, tetrahydropyranyl, dioxaborolanyl, or indolyl is preferred; in particular dioxaborolanyl, pyridyl or thiazolyl. The said heterocyclyl radicals may preferrably be unsubstituted or – depending on the substitution possibilities on the ring system - substituted by 1 to 3 substituents selected from the group consisting of halogen, =O, -OH, =S, SH, nitro, C_1-C_6alkyl, C_1-C_6hydroxyalkyl, C_1-C_6alkoxy, C_1-C_6haloalkyl, C_1-C_6haloalkoxy, phenyl and benzyl.

The invention also provides a process for preparing a compound of the formula (I) *via* a sulfinimine, nitrone or cyanide or by an Ugi reaction.

Sulfinimine

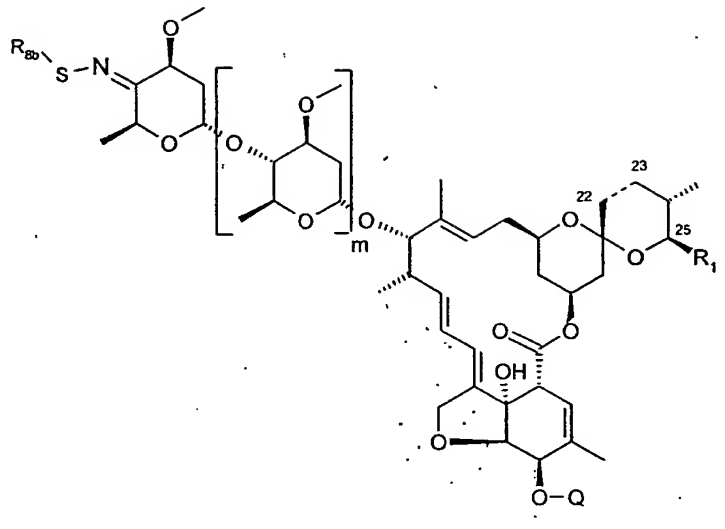
(A) Advantageously, 4" or 4' oxime avermectin or avermectin monosaccharide respectively with an oxygen protected at 5-carbon position (formula (α) below) is used as a starting material.



(α)

wherein R_1, m and the bond between carbon atoms 22 and 23 is as defined for a compound of formula (I) of the first aspect, Q is a suitable protecting group to prevent reaction on the oxygen atom at the 5-carbon position, and the double bond between the carbon atom at the 4' or 4" position and nitrogen atom is E or Z configuration.

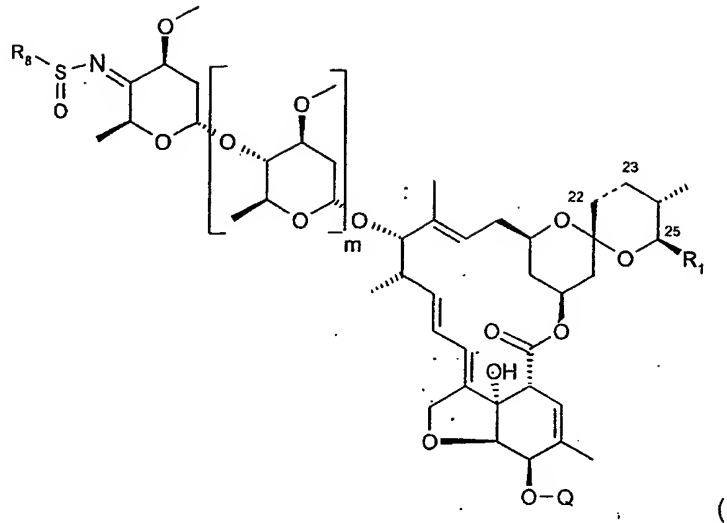
The oxime is reacted with a suitable disulfide and an aliphatic or aromatic phosphine to form the corresponding sulfenimine derivative of formula (II)



(II)

wherein R_1, m, and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I) of the first aspect, R_{8b} is as defined for R_8 in compound of formula (I) of the first aspect, Q is a suitable protecting group to prevent reaction on the oxygen atom at the 5-carbon position, and the double bond between the carbon atom at the 4' or 4" position and nitrogen atom is E or Z configuration. Derek H. Barton, William B. Motherwell, Ethan S. Simon, Samir Z. Zard *J. Chem. Soc. Trans. I* **1986**, 2243-2252 provides background on the general reaction;

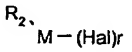
(B) the compound of formula (II) is oxidised with a suitable oxidant to form sulfinimine derivative of formula (III)



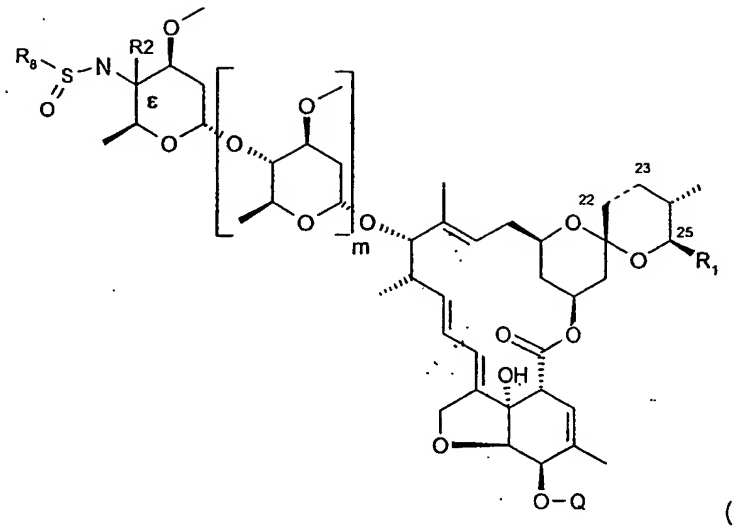
(III)

wherein R_1, m, R_8 and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I) of the first aspect, Q is a suitable protecting group to prevent reaction on the oxygen atom on 5-carbon position, and the double bond between the carbon atom at the 4' or 4" position and nitrogen atom is E or Z configuration;

(C) the compound or derivative of formula (III) is reacted with an organometallic reagent, for example, of formula



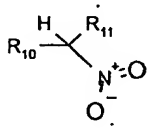
wherein R_2 is as defined for compound of formula (I) of the first aspect and M is a metal atom, preferably magnesium, lithium or cerium, and Hal is a halogen atom, preferably chlorine, bromine or iodine and r is 0 to 2 as function of the metal charge (such a reagent is known or can be prepared by methods known) to yield a sulfinamide compound of formula (IV)



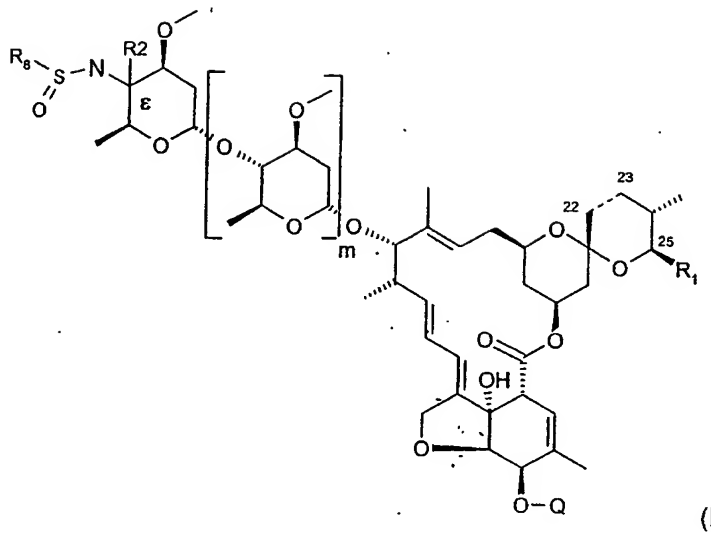
(IV)

wherein R_1, m, R_2, R_8 and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I) of the first aspect, and Q is a suitable protecting group to prevent reaction on the oxygen atom on 5-carbon position; or

(D) the compound or derivative of formula (III) is reacted with a nitro alkyl reagent, for example, of formula



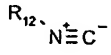
where R_{10} and R_{11} are independently of each other, H, CN, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkenyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkynyl, unsubstituted or mono- to pentasubstituted aryl, an unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl ester, an unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl ester, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl sulfone or unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl nitrile, to yield a sulfinamide compound of formula (IV)



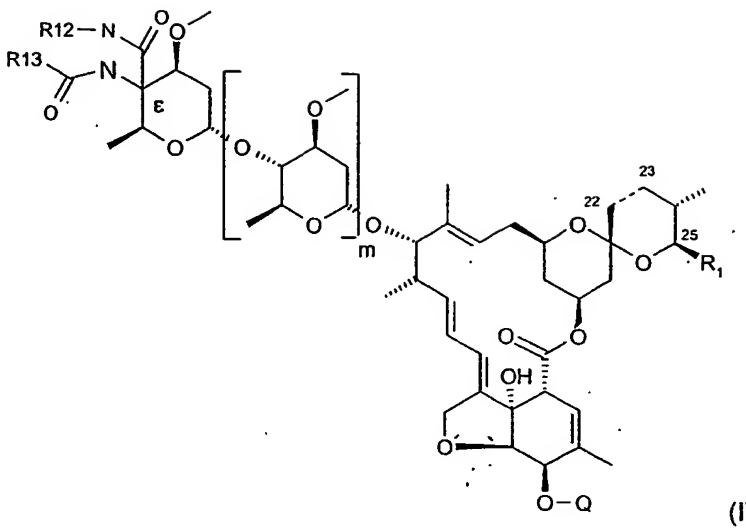
(IV)

wherein R_1, m, R_2, R_8 and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I) of the first aspect, and Q is a suitable protecting group to prevent reaction on the oxygen atom at the 5-carbon position; or

(E) the compound or derivative of formula (III) is reacted with an isocyanate reagent, for example, of formula



where R_{12} is unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkenyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkynyl, unsubstituted or mono- to pentasubstituted aryl, an unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl ester, an unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl ester, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl sulfone or unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl nitrile, to yield a amide compound of formula (IVa).

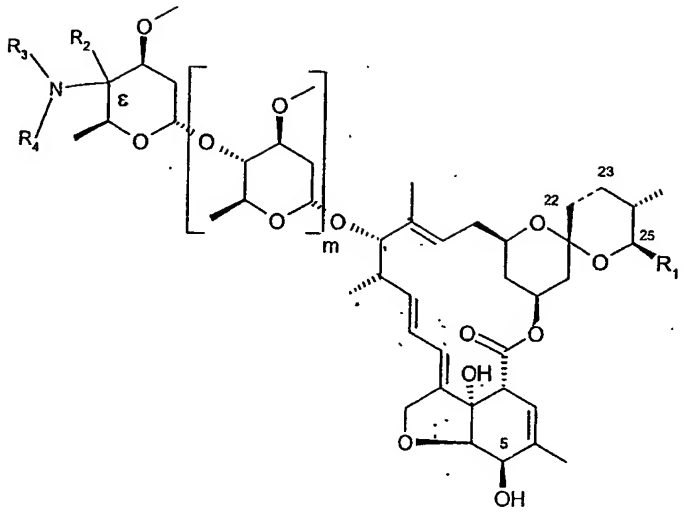


(IVa)

wherein R_1, m and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I) of the first aspect, R_{12} is as defined above, and R_{13} is unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl coming from the carboxylic acid use as reagent, and Q is a suitable protecting group to prevent reaction on the oxygen atom at the 5-carbon position; and

either

(F) the sulfinyl group and the protecting group Q are removed either in one step or one after another depending on the strength of the deprotecting agent, for example, an acidic and/or fluorine reagent, to yield a compound of formula (I)



wherein R_1, R_2, m, and the bond between carbon atoms 22 and 23 are as defined above in the first aspect, and R_3 and R_4 each represent hydrogen;

or

(G) the sulfinyl group is only removed and reactions are carried out to modify the groups R_2, R_3 and R_4, for example, by reacting a reagent of the formula R-Hal (where R is as chemical constituent, preferably R is unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkenyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkynyl, in each of these cases, one or more CH_2 groups may be replaced by C(O), C(S), C(O)O, C(S)O and Hal is halogen, especially chlorine, bromine or iodine), and thereafter removing the protecting group at oxygen atom at the 5–carbon position to yield a compound of formula (I).

or

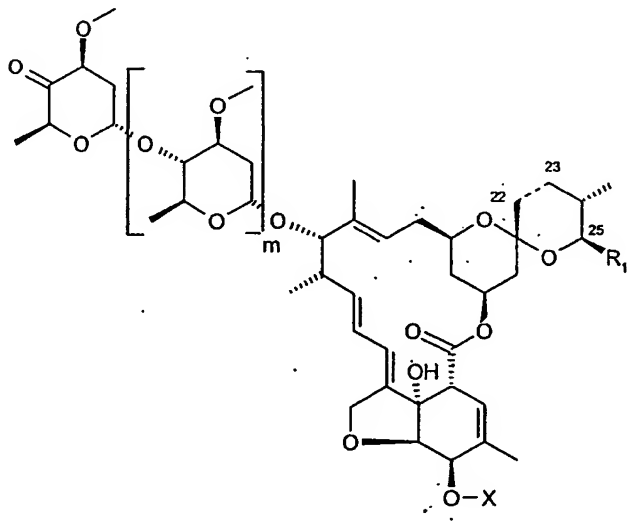
(H) if the sulfinyl group is removed during the Step before (for example during Step E), the $R_{13}C(O)$ is removed by reaction with a reducing reagent and reactions are carried out to modify the groups R_2, R_3 and R_4, for example, by reaction with a reagent of the formula R-Hal (where R is as chemical constituent, preferably unsubstituted or mono- to

pentasubstituted C_1-C_{12}alkyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkenyl or unsubstituted or mono- to pentasubstituted C_2-C_{12}alkynyl where, in each of these cases, one or more CH_2 groups may be replaced by C(O), C(S), C(O)O or C(S)O, and Hal is halogen, especially chlorine, bromine or iodine), and thereafter removing the protecting group on the oxygen atom at the 5–carbon position to yield a compound of formula (I).

In an embodiment, R_{8b} is C_1-C_6alkyl that is optionally substituted with one to five substituents selected from the group consisting of C_1-C_6alkoxy, hydroxy, and aryl, C_3-C_{12}cycloalkyl, aryl, or aryl, which, depending on the possibilities of substitution on the ring, are mono- to trisubstituted by substituents selected from the group consisting of OH, C_1-C_{12}alkyl, and C_1-C_{12}alkoxy;

Nitrone

(I) Preferably, 4" or 4' oxo avermectin or avermectin monosaccharide respectively with an oxygen protected at 5-carbon position (formula (β) below) is used as a starting material.

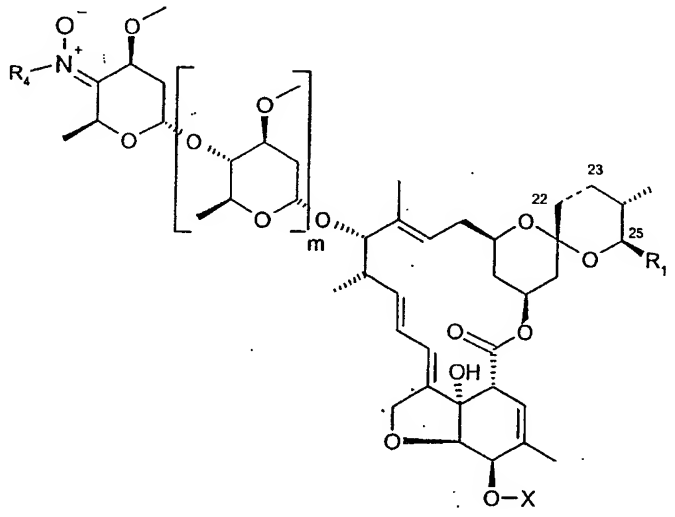


(β)

wherein R_1, m and the bond between carbon atoms 22 and 23 is as defined for a compound of formula (I) of the first aspect, and X represents H or Q (a suitable protecting group to prevent reaction of the oxygen atom at the 5-carbon position). The preparation of

such a starting material is described in EP-A-0343708, and briefly involves oxidation of the 4" or 4' hydroxyl group of avermectin or avermectin monosaccharide respectively. It is preferred that X represents Q.

The oxo derivative is reacted with a N-R_4hydroxylamine, preferably a N-hydrocarbylhydroxylamine hydrochloride, to yield a nitrone compound of formula (V)

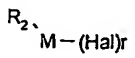


(V)

wherein R_1,R_4, m, and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I) of the first aspect, X is as defined for formula (β), and the double bond between the carbon atom at the 4' or 4" position and nitrogen atom is E or Z;

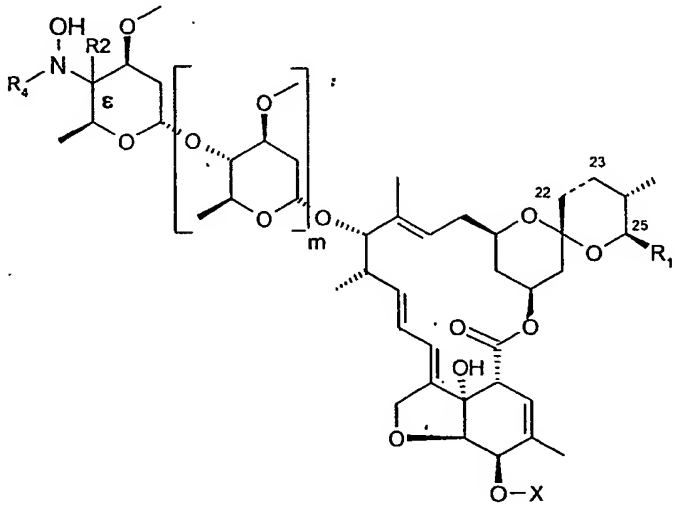
either

(J) the compound of formula (V) is reacted with an organometallic or a silyl reagent, for example, of formula



wherein R_2 is as defined for compound of formula (I) and M is a metal atom, preferably magnesium, lithium, cerium or silicon and Hal is a halogen atom, preferably chlorine,

bromine or iodine and r is 0 to 2 as function of the metal charge (such a reagent is known or can be prepared by methods known) or r is 0 in the case of silicon to yield a N-R_4hydroxyamino compound of formula (VI)



(VI)

wherein R_1, R_2, R_4, m and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I) and X is as defined for formula (β), and the *(R)* isomer at ε position is preferably obtained; and

either

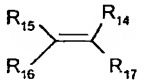
(K) remove the protecting group Q, if present, to yield a compound of formula (I), wherein R_1, R_2, R_4, m and the bond between carbon atoms 22 and 23 are as defined in the first aspect, and R_3 is OH; or

(L) carry out reactions on one or more of R_2, R_3 and R_4 groups to modify the group, for example, by reacting the compound of formula (VI) with a reagent of formula Hal-R, where R is a chemical constituent, preferably R is unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkenyl, unsubstituted or mono- to pentasubstituted

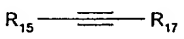
C_2-C_{12}alkynyl, in each of these cases, one or more CH_2 groups may be replaced by C(O), C(S), C(O)O, C(S)O and Hal is halogen, especially chlorine, bromine or iodine; and remove the protecting group Q, if present, to yield a compound of formula (I) wherein R_1, R_2, R_3, R_4, m and the bond between carbon atoms 22 and 23 are as defined in the first aspect, and then and removing the protecting group Q, if present, to yield a compound of formula (I);

or

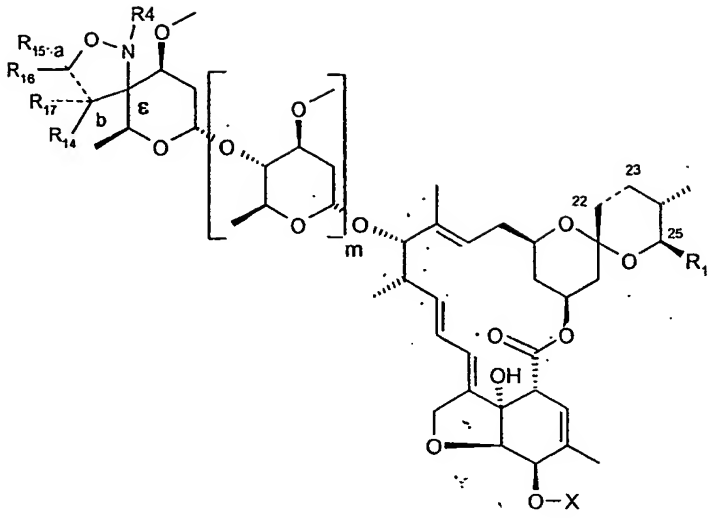
(M) the compound of formula (V) is reacted with a reagent of formula



or



where R_{14}, R_{15}, R_{16} and R_{17} are independently of each other, H, CN, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkenyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkynyl, unsubstituted or mono- to pentasubstituted aromatic, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl ester, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl ester, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl sulfone, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl nitrile, to yield a N-isoxazolidine or 2,3-dihydro-isoxazole compound of formula (VII)



(VII)

wherein R_1, R_4, m and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I), and the bond between carbon atoms a and b is a double or a single bond (depending on whether an alkene or an alkyne reagent is used) and R_{14}, R_{15}, R_{16} and R_{17} are as defined above and X is as defined for formula (β); the *(R)* isomer at ε position is preferably obtained, and the carbon a or b could *(R)* or *(S)*; and

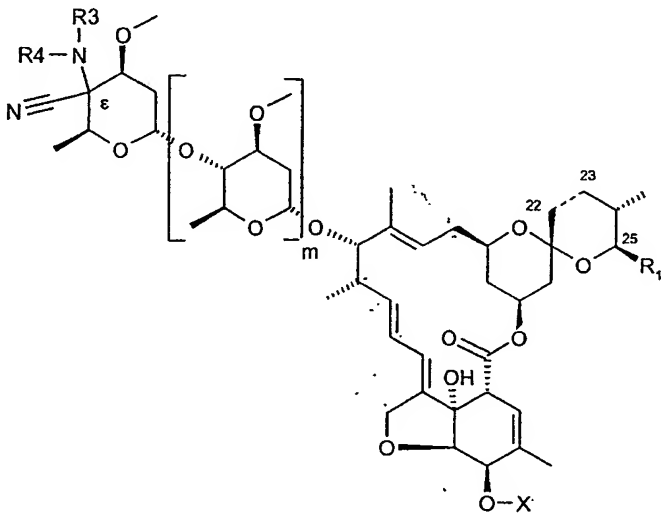
(N) remove the protecting group Q, if present, to yield a compound of formula (I), wherein R_1, R_4, m and the bond between carbon atoms 22 and 23 are as defined in the first aspect and R_2 and R_3 is an alkylene or alkenylene bridge with an oxygen atom attached to the nitrogen atom attached to the 4' or 4" position.

Cyanide

(O) Preferably, 4" or 4' oxo avermectin or avermectin monosaccharide respectively with an oxygen protected at 5-carbon position (formula (β) see F) is used as a starting material.

The compound of formula (β) is reacted with a silylated amine, such as hexamethyldisilylazane or heptamethyldisilylazane, in presence of a Lewis acid and a trialkylsilyl cyanide, such as trimethylsilyl cyanide, to yield a compound of formula (VIII).

Alternatively, the compound of formula (β) is reacted with an amine of formula R_3R_4NH, a chlorosilane, a Lewis acid and a trialkylsilyl cyanide; such as trimethylsilyl cyanide, to yield a compound of formula (VIII).



(VIII)

wherein R_1, R_3, R_4, m, and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I), X is as defined for formula (β), and the protecting group Q, if present, is removed to yield a compound of formula (I) wherein R_1, R_3, R_4, m and the bond between carbon atoms 22 and 23 are as defined in formula (I) and is R_2 is CN; or

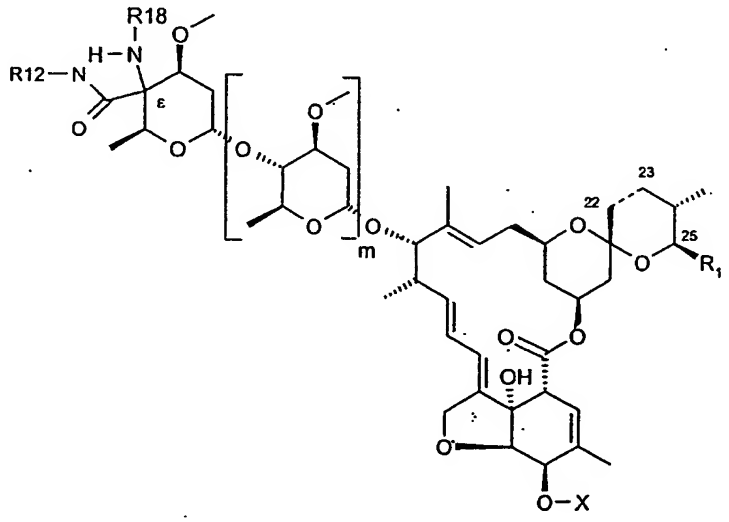
(P) carry out reactions on one or both of R_3 and R_4 groups to modify the group by reacting the compound of formula (VIII) with a reagent, such as of formula Hal-R, where R is a chemical constituent, preferably R is unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkenyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkynyl, in each of these cases, one or more CH_2 groups may be replaced by C(O), C(S), C(O)O, C(S)O and Hal is halogen, especially chlorine, bromine or iodine; and remove the protecting group Q, if present, to yield a compound of formula (I) wherein R_1, R_3, R_4, m

and the bond between carbon atoms 22 and 23 are as defined in formula (I) and is R_2 is CN.

Ugi Reaction

(Q) Preferably, 4" or 4' oxo avermectin or avermectin monosaccharide respectively with an oxygen protected at 5-carbon position (formula (β) see *I*) is used as a starting material.

The compound of formula (β) is reacted with an ammonium salt of formula $R_{18}CO_2^-NH_4^+$ (where R_{18} is H, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkenyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkynyl, unsubstituted or mono- to pentasubstituted aryl, an unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl ester, an unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl ester, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl sulfone or unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl nitrile), an isocyanide of formula $R_{12}NC$ (see E) to yield a compound of formula (IX).



(IX)

wherein R_1, m, and the bond between carbon atoms 22 and 23 are as defined for a compound of formula (I), X is as defined for formula (β), and the protecting group Q, if present, is removed to yield a compound of formula (I) wherein R_1, R_3, m and the bond between carbon atoms 22 and 23 are as defined in formula (I), R_2 is $R_{12}NHC(O)$ and R_4 is $R_{18}C(O)$.

Compounds of formula (I) can themselves be used as starting materials for further reactions so that further derivatives can be prepared, for example, by altering the groups R_2, R_3 and R_4 by suitable known reactions, such as alkylation, acylation, metathesis, palladium coupling reactions, addition of organometallics.

The preparation of avermectin monosaccharide derivatives of formula (I) follow the process steps described above, but from the corresponding monosaccharide derivative.

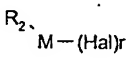
The comments made above in connection with tautomer or diastereoisomer of compound of formula (I) applies analogously to the starting materials mentioned in respect of their tautomers and diasteroisomers.

The conditions for reactions described are carried out in a manner known *per se*, for example in the absence or, customarily, in the presence of a suitable solvent or diluent or of a mixture thereof, the reactions being carried out, as required, with cooling, at room temperature or with heating, for example, in a temperature range of approximately from -80°C to the boiling temperature of the reaction medium, preferably from approximately 0°C to approximately +150°C, and, if necessary, in a closed vessel, under pressure, under an inert gas atmosphere and/or under anhydrous conditions. Especially advantageous reaction conditions can be found in the Example section.

The reaction time is not critical; a reaction time of from about 0.1 to about 24 hours, especially from about 0.5 to about 10 hours, is preferred.

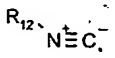
The product is isolated by customary methods, for example by means of filtration, crystallization, distillation or chromatography, or any suitable combination of such methods.

The organometallic reagent used in steps (C) and (J) of formula



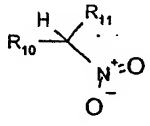
is known or can be prepared by methods known. A suitable example is a Grignard reagent.

The isocyanate reagent used in step (E) and step (Q) of formula



is known or can be prepared by methods known.

The nitroalkyl reagent used in step (D) of formula



is known or can be prepared by methods known.

It is generally useful to protect oxygen at the 5-carbon position to prevent reaction on that position when carrying out reactions with avermectin and avermectin monosaccharide. Protecting groups include: alkyl ether radicals, such as methoxymethyl, methylthiomethyl, tert-butylthiomethyl, benzyloxymethyl, p-methoxybenzyl, 2-methoxyethoxymethyl, 2,2,2-trichloroethoxymethyl, 2-(trimethylsilyl)ethoxymethyl, tetrahydropyranyl, tetrahydrofuranyl, 1-ethoxyethyl, 1-(2-chloroethoxy)ethyl, 1-methyl-1-methoxyethyl, 1-

methyl-1-benzyloxyethyl, trichloroethyl, 2-trimethylsilylethyl, tert-butyl, allyl, p-methoxyphenyl, 2,4-dinitrophenyl, benzyl, p-methoxybenzyl, o-nitrobenzyl, p-nitrobenzyl, triphenylmethyl; trialkylsilyl radicals, such as trimethylsilyl, triethylsilyl, dimethyl-tert-butylsilyl, dimethyl-isopropylsilyl, dimethyl-1,1,2-trimethylpropylsilyl, diethyl-isopropylsilyl, dimethyl-tert-hexylsilyl, but also phenyl-tert-alkylsilyl groups, such as diphenyl-tert-butylsilyl; esters, such as formates, acetates, chloroacetates, dichloroacetates, trichloroacetates, trifluoroacetates, methoxyacetates, phenoxyacetates, pivaloates, benzoates; alkyl carbonates, such as methyl-, 9-fluorenylmethyl-, ethyl-, 2,2,2-trichloroethyl-, 2-(trimethylsilyl)ethyl-, vinyl-, allyl-, benzyl-, p-methoxybenzyl-, o-nitrobenzyl-, p-nitrobenzyl-, but also p-nitrophenyl-carbonate.

Preference is given to trialkylsilyl radicals, such as trimethylsilyl, triethylsilyl, dimethyl-tert-butylsilyl, diphenyl-tert-butylsilyl, esters, such as methoxyacetates and phenoxyacetates, and carbonates, such as 9-fluorenylmethylcarbonates and allylcarbonates. Dimethyl-tert-butylsilyl ether is especially preferred.

Once the desired reactions are completed, the reagents used for removing the protecting group depends on the strength of the protecting group used. There are suitable for the removal of the protecting group Lewis acids, such as hydrochloric acid, methanesulfonic acid, BF_3*OEt_2, HF in pyridine, $Zn(BF_4)_2$*H_2O, p-toluenesulfonic acid, $AlCl_3$, $HgCl_2$; ammonium fluoride, such as tetrabutylammonium fluoride; bases, such as ammonia, trialkylamine or heterocyclic bases; hydrogenolysis with a catalyst, such as palladium-on-carbon; reducing agents, such as sodium borohydride or tributyltin hydride with a catalyst, such as $Pd(PPh_3)_4$, or also zinc with acetic acid. Preference is given to acids, such as methanesulfonic acid or HF in pyridine; sodium borohydride with Pd(0); bases, such as ammonia, triethylamine or pyridine; especially acids, such as HF in pyridine or methanesulfonic acid. Generally, an acidic reagent, such as a mixture of methanesulfonic acid in methanol or a HF in pydrine, is effective in removing dimethyl-tert-butylsilyl ether group from oxygen at the 5-carbon position. A less acidic reagent, such as a mixture of alcohol (*e.g.*, isopropanol) and trifluroacetic acid in a solvent (*e.g.*, THF), is not adequate, but it is generally sufficient to remove the sulfinyl group in step (F)

The starting materials mentioned that are used for the preparation of the compound of formula (I), the intermediates therefor (*e.g.*, the compound of formula (II), (III) or (V)), and, where applicable, their tautomers are known or can be prepared by methods known *per se*.

The process steps (A) to (Q) described above are detailed further below:

Process step (A):

Examples of solvents and diluents include: aromatic, aliphatic and alicyclic hydrocarbons and halogenated hydrocarbons, such as benzene, toluene, xylene, mesitylene, tetralin, chlorobenzene, dichlorobenzene, bromobenzene, petroleum ether, hexane, cyclohexane, dichloromethane, trichloromethane, tetrachloromethane, dichloroethane, trichloroethene or tetrachloroethene; ethers, such as diethyl ether, dipropyl ether, diisopropyl ether, dibutyl ether, tert-butyl methyl ether, ethylene glycol monomethyl ether, ethylene glycol monoethyl ether, ethylene glycol dimethyl ether, dimethoxydiethyl ether, tetrahydrofuran or dioxane; esters of carboxylic acids, such as ethyl acetate; amides, such as dimethylformamide, dimethylacetamide or 1-methyl-2-pyrrolidinones; nitriles, such as acetonitrile; nitroalkyls, such as nitromethane; sulfoxides, such as dimethyl sulfoxide; or mixtures of the mentioned solvents. Preference is given to ether, such as tetrahydrofuran and diethyl ether, especially tetrahydrofuran.

The reactions are advantageously carried out in a temperature range of from approximately -70°C to 50°C, preferably at from -10°C to 25°C.

A preferred disulfide is a carbon-containing disulfide, for example, dialiphatic disulfide, dialicyclic disulfide, diaromatic disulfide, such as di-tert-butyl disulfide, di-tert-amyl disulfide, di-tert-dodecyl disulfide , diphenyl disulfide, p-tolyl disulfide, especially preferred is diphenyl disulfide.

A preferred phosphine is trialkylphosphine, triarylphosphine, such as tributylphosphine, triethylphosphine, triphenylphosphine, especially preferred is tributylphosphine.

Especially preferred conditions for the reaction are described in Example P1 (step A).

Process step (B):

Examples of solvents and diluents are the same as those mentioned under Process step A. In particular, halogenated hydrocarbons, such as chloroform and dichloromethan and water are especially suitable.

The reactions are advantageously carried out in a temperature range of from approximately -70°C to 50°C, preferably at from -10°C to 25°C.

Examples of oxidant suitable for oxidizing the sulfenimine to a sulfinimine are hydrogen peroxide, arylperoxoic acid, alkyl hydroperoxide, dimethyldioxirane, potassium peroxymonosulfate sulfate, sodium periodate, bialkylperoxide, 2-iodylbenzoic acid, α-Cumene hydroperoxide, oxaziridine analogues; preferred is metachloroperbenzoic acid. The reaction is preferably carried out in biphasic system.

Especially preferred conditions for the reaction are described in Example P1 (step B).

Process step (C):

Examples of solvents and diluents are the same as those mentioned under Process step A. Preference is given to ether, such as tetrahydrofuran and diethyl ether, especially tetrahydrofuran.

The reactions are advantageously carried out in a temperature range of from approximately -100°C to 50°C, preferably at from -78°C to 25°C.

Especially preferred conditions for the reaction are described in Examples P1 (step C) or P2 (step A).

Process step (D):

Examples of solvents and diluents are the same as those mentioned under Process step A. Preference is given to the use of the nitroalkyl reagent as solvent.

Suitable bases are especially carbonates, such as sodium carbonate, sodium hydrogen carbonate, potassium carbonate, trialkylamines, such as triethylamine, dialkylamines, such as piperidine, and heterocyclic bases, such as pyridine.

The reactions are advantageously carried out in a temperature range of from approximately -70°C to 70°C, preferably at from -25°C to 50°C.

Especially preferred conditions for the reaction are described in Examples P21 (step A) or P23 (step A).

The process step for the removing of the protecting group Q is identical to the Process step (F).

Process step (E):

Examples of solvents and diluents are the same as those mentioned under Process step A. Preference is given to polychloroalkane, such as dichloromethane.

Suitable bases are especially carbonates, such as sodium carbonate, sodium hydrogen carbonate, potassium carbonate, trialkylamines, such as triethylamine, dialkylamines, such as piperidine, and heterocyclic bases, such as pyridine.

Suitable acids are especially polyhalogenated carboxylic acid, such as trifluoroacetic acid, chloroacetic acid, dichloroacetic acid, trichloroacetic acid.

The reactions are advantageously carried out in a temperature range of from approximately -80°C to 70°C, preferably at from -80°C to 50°C.

The process step for the removing of the protecting group Q is identical to the Process step (F).

Especially preferred conditions for the reaction are described in Examples P22 (step A).

Process step (F):

Examples of solvents and diluents are the same as those mentioned under Process step A. In addition, alcohols, such as methanol, ethanol or 2-propanol, and water are suitable.

Suitable acids are especially polyhalogened carboxylic acid, such as trifluoroacetic acid, chloroacetic acid, dichloroacetic acid, trichloroacetic acid; or alkylsulfonic acid, such as methanesulfonic acid; or source of anionic fluoride, such as hydrofluoric acid, tetrabutylammonium fluoride, potassium fluoride, cesium fluoride.

The reactions are advantageously carried out in a temperature range of from approximately -100°C to 50°C, preferably at from -78°C to 25°C.

Especially preferred conditions for the reaction are described in Examples P1 (step D), P1 (step E), and P2 (step B).

Process step (G):

Examples of solvents and diluents are the same as those mentioned under Process step (A). Preference is given to ether, such as tetrahydrofuran, and halogenated hydrocarbons, such as dichloromethane and esters of carboxylic acids, such as ethyl acetate and mixture of halogenated hydrocarbons and water and mixture of esters of carboxylic acids and water.

The reactions are advantageously carried out in a temperature range of approximately from -10°C to 120°C, preferably at from 20°C to 100°C.

Suitable bases are especially carbonates, such as sodium carbonate, sodium hydrogen carbonate, potassium carbonate, trialkylamines, such as triethylamine, and heterocyclic bases, such as pyridine or dimethylaminopyridine.

Especially preferred conditions for the reaction are described in Examples P5 (step A), P8 (step A), P9 (step A), P11 (step A), P12 (step A).

And the process step for the removing of the protecting group Q is identical to the Process step (F).

Process step (H):

Examples of solvents and diluents are the same as those mentioned under Process step (A). Preference is given to ethers, such as tetrahydrofuran, halogenated hydrocarbons, such as dichloromethane and esters of carboxylic acids, such as ethyl acetate, and to mixtures of halogenated hydrocarbons and water and mixtures of esters of carboxylic acids and water.

The reactions are advantageously carried out in a temperature range of approximately from -10°C to 120°C, preferably at from 20°C to 100°C.

Suitable reducing reagents are borane derivatives such as sodium borohydride and sodium cyanoborohydrate.

Suitable bases are especially carbonates, such as sodium carbonate, sodium hydrogen carbonate, potassium carbonate, trialkylamines, such as triethylamine, and heterocyclic bases, such as pyridine or dimethylaminopyridine.

The process step for the removing of the protecting group Q is identical to the Process step (F).

Especially preferred conditions for the reaction are described in Examples P30 (step A, B).

Process step (I):

Examples of solvents and diluents are the same as those mentioned under Process step A. In addition, alcohols, such as methanol, ethanol or 2-propanol, are suitable. Preference is given to alcohols, such as methanol.

Examples of R_4hydroxyamines are N-alkylhydroxylamines. N- cycloalkylhydroxylamines, N-arylhydroxylamines, N-benzylhydroxylamines, N-heteroarylhydroxylamines; specific examples include N-methylhydroxylamine.

Suitable bases are especially trialkylamines, such as triethylamine, and heterocyclic bases, such as pyridine.

The reactions are advantageously carried out in a temperature range of from approximately -70°C to 50°C, preferably at from -10°C to 40°C.

Especially preferred conditions for the reaction are described in Examples P3 (step A).

Process step (J):

Conditions described in Process step (C) are also applicable.

Especially preferred conditions for the reaction step are described in Example P3 (step B).

Process step (K):

Conditions described in Process step (F) are also applicable.

Especially preferred conditions for the reaction are described in Examples P3 (step C).

Process step (L):

Examples of solvents and diluents are the same as those mentioned under Process step (A). Preference is given to ether, such as tetrahydrofuran, and halogenated hydrocarbons, such as dichloromethane and esters of carboxylic acids, such as ethyl acetate and mixture of halogenated hydrocarbons and water and mixture of esters of carboxylic acids and water.

Suitable examples of R-Hal include alkyl halides, such as methyl iodine, and acyl halides such as acetyl chloride, and sulfonyl halide, such as sulfamoyl chloride or benzenesulfonyl

chloride or methylsulfonyl chloride, and arylchloroformate, alkyl haloformate, such as methylchloroformate.

The reactions are advantageously carried out in a temperature range of approximately from -10°C to 120°C, preferably at from 20°C to 100°C.

Suitable bases are especially carbonates, such as sodium carbonate, sodium hydrogen carbonate, potassium carbonate, trialkylamines, such as triethylamine, and heterocyclic bases, such as pyridine.

Especially preferred conditions for the reaction are described in Example P7.

Process step (M):

Examples of solvents and diluents are the same as those mentioned under Process step (A). Preference is given to aromatic, such as toluene.

The reactions are advantageously carried out in a temperature range of approximately from -10°C to 150°C, preferably at from 0°C to 100°C.

Especially preferred conditions for the reaction are described in Examples P6 (step A).

Process step (N):

Conditions described in Process step (F) are also applicable.

Especially preferred conditions for the reaction are described in Examples P6 (step B).

Process step (O):

Examples of solvents and diluents are the same as those mentioned under Process step A. Preference is given to ester, such as ethyl acetate and to aromatic, such as toluene.

Suitable Lewis acids, for example, are aluminium chloride, tin tetrachloride, ferric chloride, boron trichloride, titanium chloride especially zinc derivatives, such as zinc chloride.

In alternative process, the amine is silylated *in situ* by addition of trialkylsilyl chloride, such as trimethylsilyl chloride.

The reactions are advantageously carried out in a temperature range of from approximately -70°C to 50°C, preferably at from -10°C to 100°C.

Especially preferred conditions for the reaction are described in Examples P15 (step A), P16 (step A), P17 (step A), P18 (step A).

Process step (P):

Examples of solvents and diluents are the same as those mentioned under Process step (A). Preference is given to ether, such as tetrahydrofuran, and halogenated hydrocarbons, such as dichloromethane and esters of carboxylic acids, such as ethyl acetate and mixture of halogenated hydrocarbons and water and mixture of esters of carboxylic acids and water.

The reactions are advantageously carried out in a temperature range of approximately from -10°C to 120°C, preferably at from 20°C to 100°C.

Suitable bases are especially carbonates, such as sodium carbonate, sodium hydrogen carbonate, potassium carbonate, trialkylamines, such as triethylamine, and heterocyclic bases, such as pyridine.

Especially preferred conditions for the reaction are described in Example P19 and P20.

Process step (Q):

Examples of solvents and diluents are the same as those mentioned under Process step A. In addition, alcohols, such as methanol, ethanol or 2-propanol, are suitable. Preference is given to alcohols, such as methanol.

Suitable ammonium salts are especially ammonium salts derived from formic acid, alkyl carboxylic acid, such as acetic acid and polyhalogenated carboxylic acid, such as trifluoroacetic acid, chloroacetic acid, dichloroacetic acid and trichloroacetic acid.

The reactions are advantageously carried out in a temperature range of from approximately -80°C to 70°C, preferably at from -20°C to 50°C.

The compound of the invention may be in the form of one of possible isomers. Therefore, a preparation can result in mixture of isomers, *i.e.*, a diastereomeric mixture; the invention relates both to a pure isomer and to a diastereomeric mixture and is to be interpreted accordingly, even if stereochemical details are not mentioned specifically in every case.

A diastereomeric mixture can be resolved into the pure isomers by known methods, for example by recrystallisation from a solvent, by chromatography, for example, high pressure liquid chromatography (HPLC) on acetylcellulose, with the aid of suitable microorganisms, by cleavage with specific, immobilised enzymes; or *via* the formation of inclusion compounds, for example using crown ethers, only one isomer being complexed.

Apart from by separation of corresponding mixtures of isomers, pure diastereoisomers can be obtained according to the invention also by generally known methods of stereoselective

synthesis, for example by carrying out the process according to the invention using starting materials having correspondingly suitable stereochemistry.

In each case it may be advantageous to isolate or synthesise the biologically more active isomer, where the individual components have different biological activity.

The compound of formulae (I) to (IX) may also be obtained in the form of their hydrates and/or may include other solvents, for example solvents that may have been used for the crystallisation of compounds in solid form.

The invention relates to all those embodiments of the process according to which a compound obtainable as starting material or intermediate at any stage of the process is used as starting material and some or all of the remaining steps are carried out or a starting material is used in the form of a derivative or salt and/or diastereoisomers, or, especially, is formed under the reaction conditions. For instance a compound of formula (I) can be used as a starting material for the preparation of another compound of formula (I). Such manipulation methods are known to those skilled in the art.

In the processes of the present invention it is preferable to use those starting materials and intermediates, which result in a compound of formula (I).

The invention relates especially to the preparation processes described in Examples P1 to P30.

Also within the scope of the present invention is a compound of formula (I) having a protecting group on the oxygen atom at the 5-carbon position instead of being a hydroxy group. In the event the protecting group is hydrolysable under mild conditions (such protecting groups include, for example unsubstituted or mono- to pentasubstituted

C_1-C_{12}alkylcarbonates) or is a hydrocarbyl or substituted derivative thereof (such as, a unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl, in which one or more carbon atoms can be replaced by one or more oxygen atoms).

The compounds of formulae (II) to (VIII) also form part of the present invention. The compounds of formulae (II) to (VIII) may have either a protecting group on the oxygen atom at the 5-carbon position, or alternatively are deprotected, preferably each has a protecting group to protect the oxygen atom at the 5-carbon position. In the event, compounds of formulae (IV), (VI), (VII) and (VIII) are deprotected and a hydroxy group is bound to the 5-carbon position, such compounds are within the scope of formula (I).

Compounds of formulae (III) and (V) in a protected or unprotected form also show pesticidal activity, especially in the event where the protecting group is not present (*i.e.*, hydroxy group at the 5-carbon position) or where the protecting group is hydrolysable under mild conditions (such protecting groups include, for example unsubstituted or mono- to pentasubstituted C_1-C_{12}alkylcarbonate).

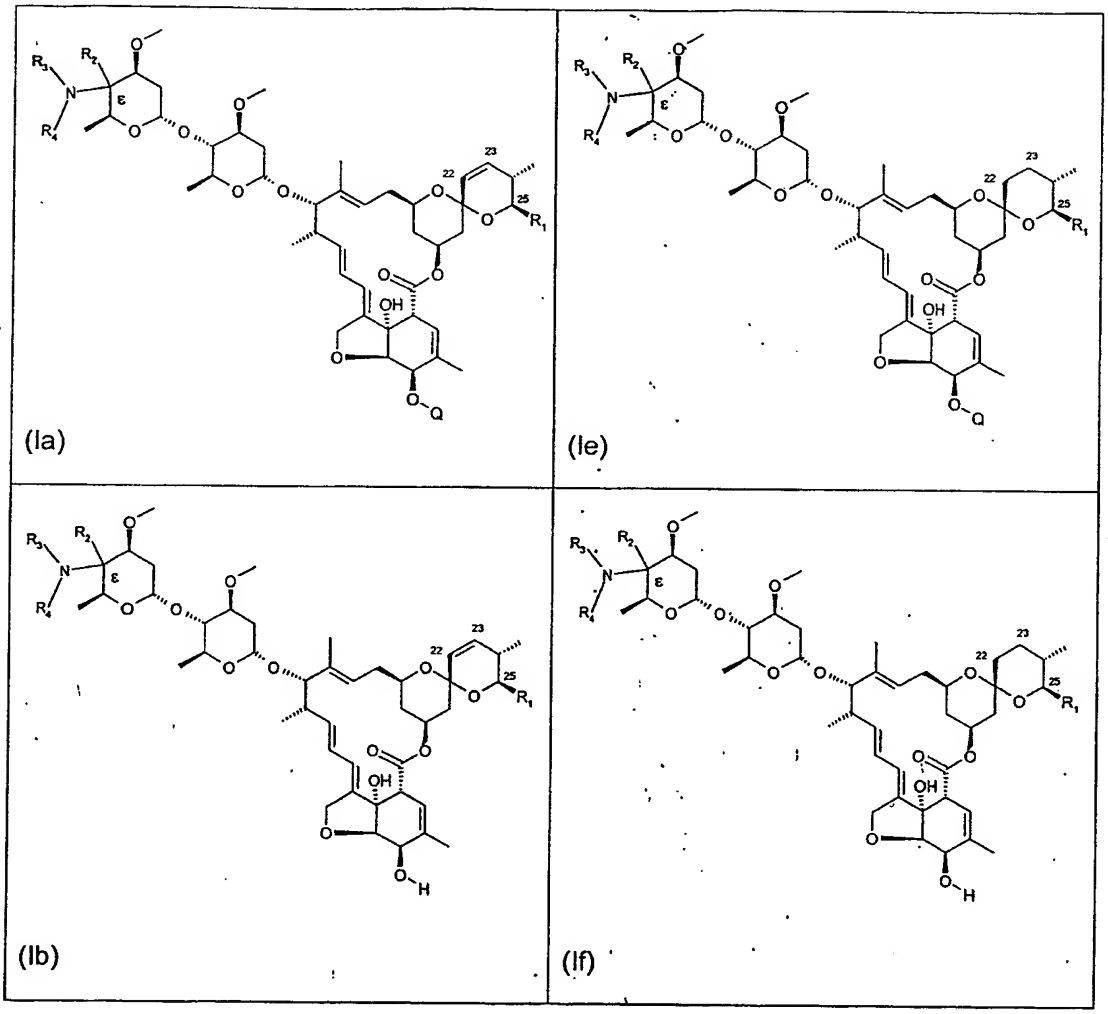
The compounds of the formulae (II) to (VIII), in particular (III) and (V), in both the protected and deprotected form are intermediates for the synthesis of compounds of formula (I). The use, therefore, of compounds of formula (II) to (VIII) in both the protected and deprotected form for the synthesis of compounds of formula (I) is also a subject of this invention. The preferences for the substituent groups, as appropriate, are the same as defined for the compound of the formula (I) in groups (2) to (22).

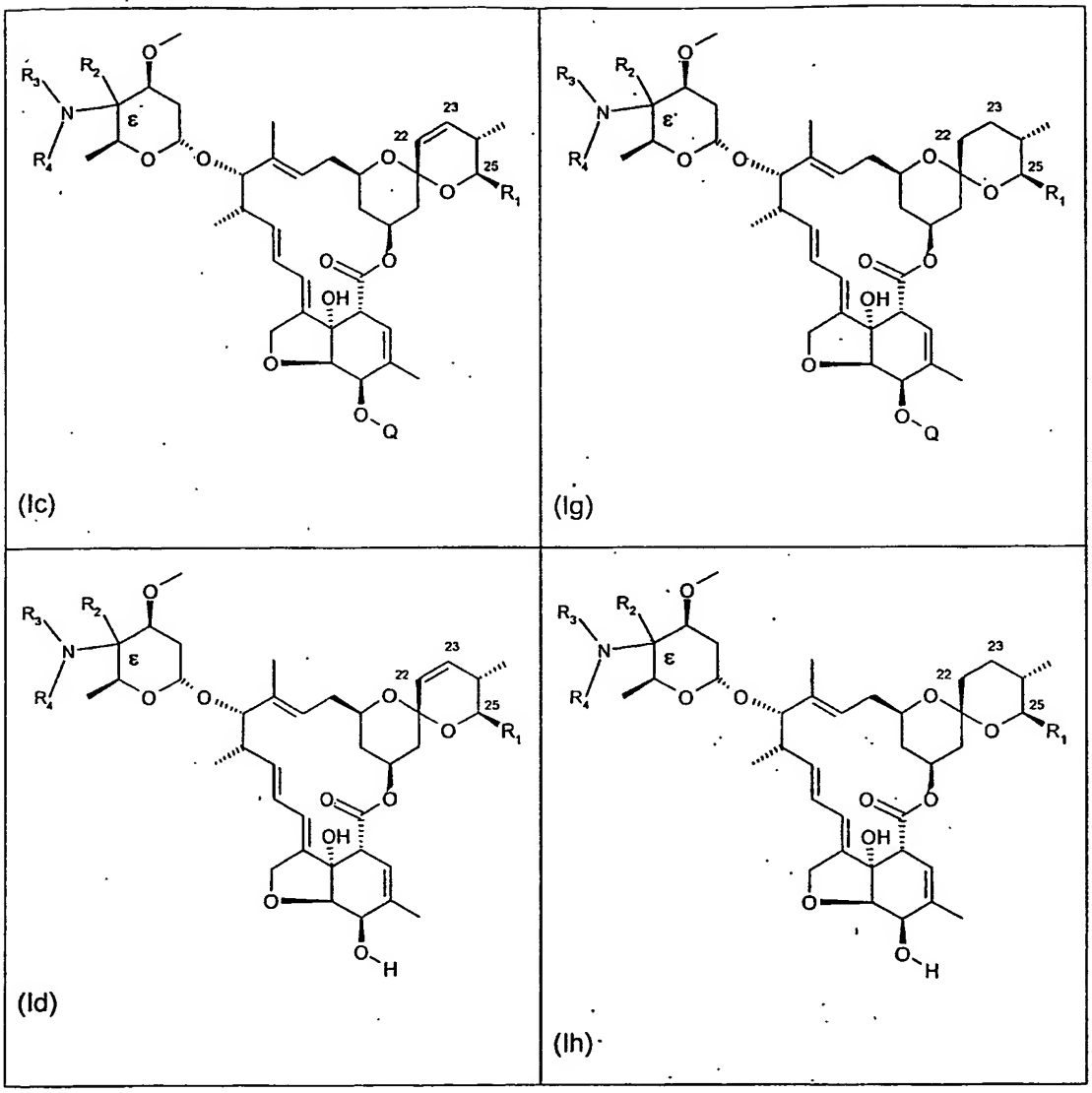
In the context of the invention, a reference is made to:

- compounds of formulae (Ia to Ih) of Table X and Tables 1 to 48;
- compounds of formulae (IIIa to IIId) of Table Y and Tables 49 to 72 ; and

- compounds of formulae (Va to Vd) of Table Z and Tables 73 to 96 ; and in each case, if appropriate, to its E / Z isomer or a mixture thereof.

Table X: A compound of any one of the formulae (Ia) to (Ih)



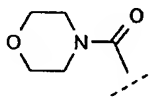


where, for each formula

Line	R_2	R_3	R_4
1	CF_3	OH	CH_3
2	CF_3	OH	Et
3	CF_3	H	H
4	CF_3	$CH_3C(O)$	H
5	CF_3	HC(O)	H

Line	R_2	R_3	R_4
6	CF_3	CH_3	CH_3
7	CF_3	$CH_3OC(O)$	H
8	CF_3	$CH_3CH_2OC(O)$	H
9	CF_3	$CH_3OCH_2C(O)$	H
10	CF_3	H	CH_3
11	CF_3	$CH_3C(O)$	CH_3
12	CF_3	HC(O)	CH_3
13	CF_3	$CH_3OC(O)$	CH_3
14	CF_3	$CH_3CH_2OC(O)$	CH_3
15	CF_3	$CH_3OCH_2C(O)$	CH_3
16	CH_3CH_2	OH	CH_3
17	CH_3CH_2	OH	Et
18	CH_3CH_2	H	H
19	CH_3CH_2	$CH_3C(O)$	H
20	CH_3CH_2	HC(O)	H
21	CH_3CH_2	CH_3	CH_3
22	CH_3CH_2	$CH_3OC(O)$	H
23	CH_3CH_2	$CH_3CH_2OC(O)$	H
24	CH_3CH_2	$CH_3OCH_2C(O)$	H
25	CH_3CH_2	H	CH_3
26	CH_3CH_2	$CH_3C(O)$	CH_3
27	CH_3CH_2	HC(O)	CH_3
28	CH_3CH_2	$CH_3OC(O)$	CH_3
29	CH_3CH_2	$CH_3CH_2OC(O)$	CH_3
30	CH_3CH_2	$CH_3OCH_2C(O)$	CH_3
31	CH_3	$C(O)CH_2CH_2C(O)$	
32	CF_3	$C(O)CH_2CH_2C(O)$	
33	CH_3CH_2	$C(O)CH_2CH_2C(O)$	

Line	R_2	R_3	R_4
34	Vinyl	$C(O)CH_2CH_2C(O)$	
35	Allyl	$C(O)CH_2CH_2C(O)$	
36	CH_3	$C(O)CH_2CH_2\ CH_2$	
37	CF_3	$C(O)CH_2CH_2\ CH_2$	
38	CH_3CH_2	$C(O)CH_2CH_2\ CH_2$	
39	Vinyl	$C(O)CH_2CH_2\ CH_2$	
40	Allyl	$C(O)CH_2CH_2\ CH_2$	
41	$C(O)CH_2CH_2\ CH_2$		H
42	$C(O)CH_2CH_2\ CH_2$		$C(O)CH_3$
43	$C(O)CH_2CH_2\ CH_2$		C(O)H
44	$C(O)CH_2CH_2\ CH_2$		$C(O)CH_2OCH_3$
45	$C(O)CH_2CH_2\ CH_2$		$C(O)OCH_3$
46	$C(O)CH_2CH_2\ CH_2$		CH_3
47	$C(O)CH_2CH_2\ CH_2$		CH_2CH_3
48	$C(O)CH_2CH_2\ CH_2$		CH_2OCH_3
49	$C(O)CH_2CH_2\ CH_2$		$CH_2O\ CH_2CH_3$
50	$C(O)CH_2CH_2\ CH_2$		SO_2NH_2
51	CH_3	$C(O)N(CH_3)_2$	H
52	CH_3	$C(O)N(CH_3)_2$	CH_3
53	CH_3	$C(S)\ CH_3$	H
54	CH_3	$C(S)\ CH_3$	CH_3
55	CH_3	S(O)Ph	H
56	CH_3	S(O)Ph	CH_3
57	CH_3	$S(O)_2Ph$	H
58	CH_3	$S(O)_2Ph$	CH_3
59	CH_3	$CH_2C(O)CH_3$	H
60	CH_3	$CH_2C(O)CH_3$	CH_3

Line	R_2	R_3	R_4
61	CH_3	$CH_2C(O)NH(CH_3)$	H
62	CH_3	$CH_2C(O)NH(CH_3)$	CH_3
63	CH_3	$CH_2C(O)O\ CH_3$	H
64	CH_3	$CH_2C(O)O\ CH_3$	CH_3
65	CH_3	$CH_3C(O)$	CH_3
66	CH_3	HC(O)	CH_3
67	CH_3	$CH_3OC(O)$	CH_3
68	CH_3	$CH_3CH_2OC(O)$	CH_3
69	CH_3	$N(CH_3)_2$	CH_3
70	CN	$CH_2C(CH_3)C(O)$	CH_3
71	CN	$CH_2CHC(O)$	H
72	CN	$(CH_3)_2NC(O)$	H
73	CN	$CH_3CHCHC(O)$	H
74	CN	$CH_2CH(CH_3)C(O)$	H
75	CN	$(CH_3)_2NC(O)$	H
76	CN	$(CH_3)_2CHC(O)$	H
77	CN	cyclobutylC(O)	H
78	CN	$CH_3CH_2SC(O)$	H
79	CN		H

and

Table 1	A compound of the formula (Ia) wherein R_1 is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 2	A compound of the formula (Ia) wherein R_1 is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.

Table 3	A compound of the formula (Ia) wherein R_1 is cyclohexyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 4	A compound of the formula (Ia) wherein R_1 is cyclohexyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 5	A compound of the formula (Ia) wherein R_1 is 1-methyl butyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 6	A compound of the formula (Ia) wherein R_1 is 1-methyl butyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 7	A compound of the formula (Ib) wherein R_1 is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 8	A compound of the formula (Ib) wherein R_1 is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 9	A compound of the formula (Ib) wherein R_1 is cyclohexyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 10	A compound of the formula (Ib) wherein R_1 is cyclohexyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 11	A compound of the formula (Ib) wherein R_1 is 1-methyl butyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 12	A compound of the formula (Ib) wherein R_1 is 1-methyl butyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 13	A compound of the formula (Ic) wherein R_1 is sec-butyl or isopropyl, the configuration of

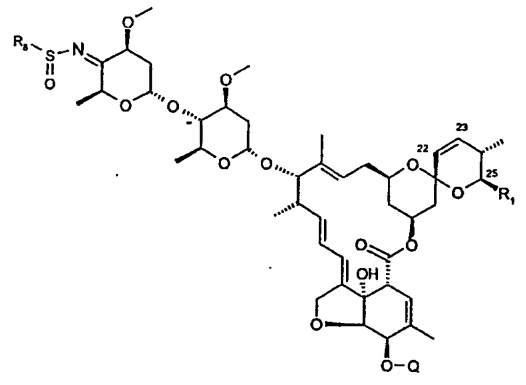
	the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 14	A compound of the formula (Ic) wherein R_1 is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 15	A compound of the formula (Ic) wherein R_1 is cyclohexyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 16	A compound of the formula (Ic) wherein R_1 is cyclohexyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 17	A compound of the formula (Ic) wherein R_1 is 1-methyl butyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 18	A compound of the formula (Ic) wherein R_1 is 1-methyl butyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 19	A compound of the formula (Id) wherein R_1 is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 20	A compound of the formula (Id) wherein R_1 is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 21	A compound of the formula (Id) wherein R_1 is cyclohexyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 22	A compound of the formula (Id) wherein R_1 is cyclohexyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 23	A compound of the formula (Id) wherein R_1 is 1-methyl butyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a

	line 1 to 79 of Table X.
Table 24	A compound of the formula (Id) wherein R_1 is 1-methyl butyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 25	A compound of the formula (Ie) wherein R_1 is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 26	A compound of the formula (Ie) wherein R_1 is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 27	A compound of the formula (Ie) wherein R_1 is cyclohexyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 28	A compound of the formula (Ie) wherein R_1 is cyclohexyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 29	A compound of the formula (Ie) wherein R_1 is 1-methyl butyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 30	A compound of the formula (Ie) wherein R_1 is 1-methyl butyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 31	A compound of the formula (If) wherein R_1 is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 32	A compound of the formula (If) wherein R_1 is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 33	A compound of the formula (If) wherein R_1 is cyclohexyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.

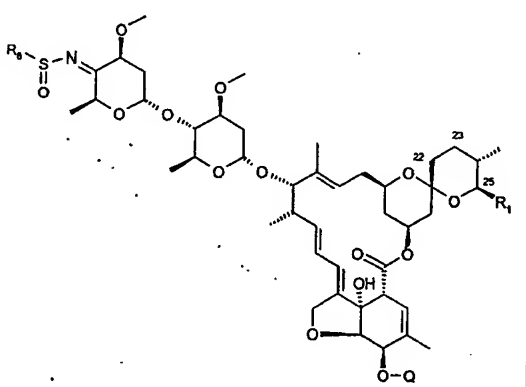
Table 34	A compound of the formula (If) wherein R_1 is cyclohexyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 35	A compound of the formula (If) wherein R_1 is 1-methyl butyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 36	A compound of the formula (If) wherein R_1 is 1-methyl butyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 37	A compound of the formula (Ig) wherein R_1 is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 38	A compound of the formula (Ig) wherein R_1 is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 39	A compound of the formula (Ig) wherein R_1 is cyclohexyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 40	A compound of the formula (Ig) wherein R_1 is cyclohexyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 41	A compound of the formula (Ig) wherein R_1 is 1-methyl butyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 42	A compound of the formula (Ig) wherein R_1 is 1-methyl butyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 43	A compound of the formula (Ih) wherein R_1 is sec-butyl or isopropyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 44	A compound of the formula (Ih) wherein R_1 is sec-butyl or isopropyl, the configuration of

	the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 45	A compound of the formula (Ih) wherein R_1 is cyclohexyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 46	A compound of the formula (Ih) wherein R_1 is cyclohexyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 47	A compound of the formula (Ih) wherein R_1 is 1-methyl butyl, the configuration of the carbon atom at the ε position is *(R)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.
Table 48	A compound of the formula (Ih) wherein R_1 is 1-methyl butyl, the configuration of the carbon atom at the ε position is *(S)*, and the substituents R_2, R_3 and R_4 corresponds to a line 1 to 79 of Table X.

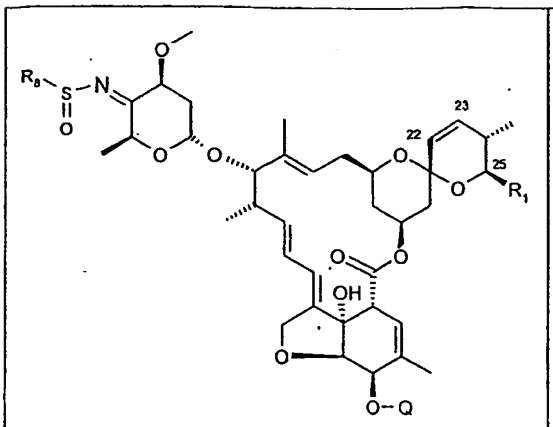
Table Y: A compound of any one of the formulae (IIIa to IIId)



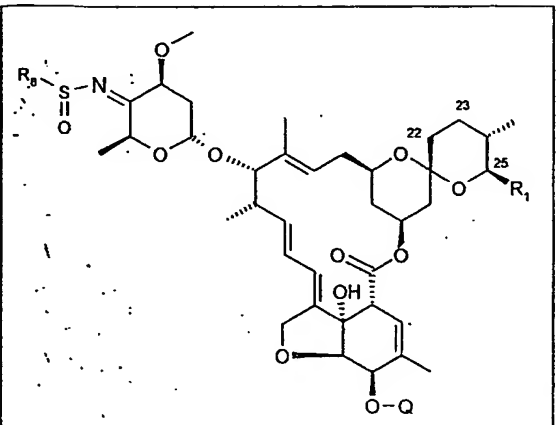
(IIIa)



(IIIc)



(IIIb)



(IIId)

where

Line	R_8	Q
1	Ph	$SiMe_2tBu$
2	Ph	Me
3	Ph	$C(O)CH_3$
4	Ph	CH_2OCH_3
5	Ph	$C(O)OCH_3$
6	Ph	$C(O)OCH_2CHCH_2$

and

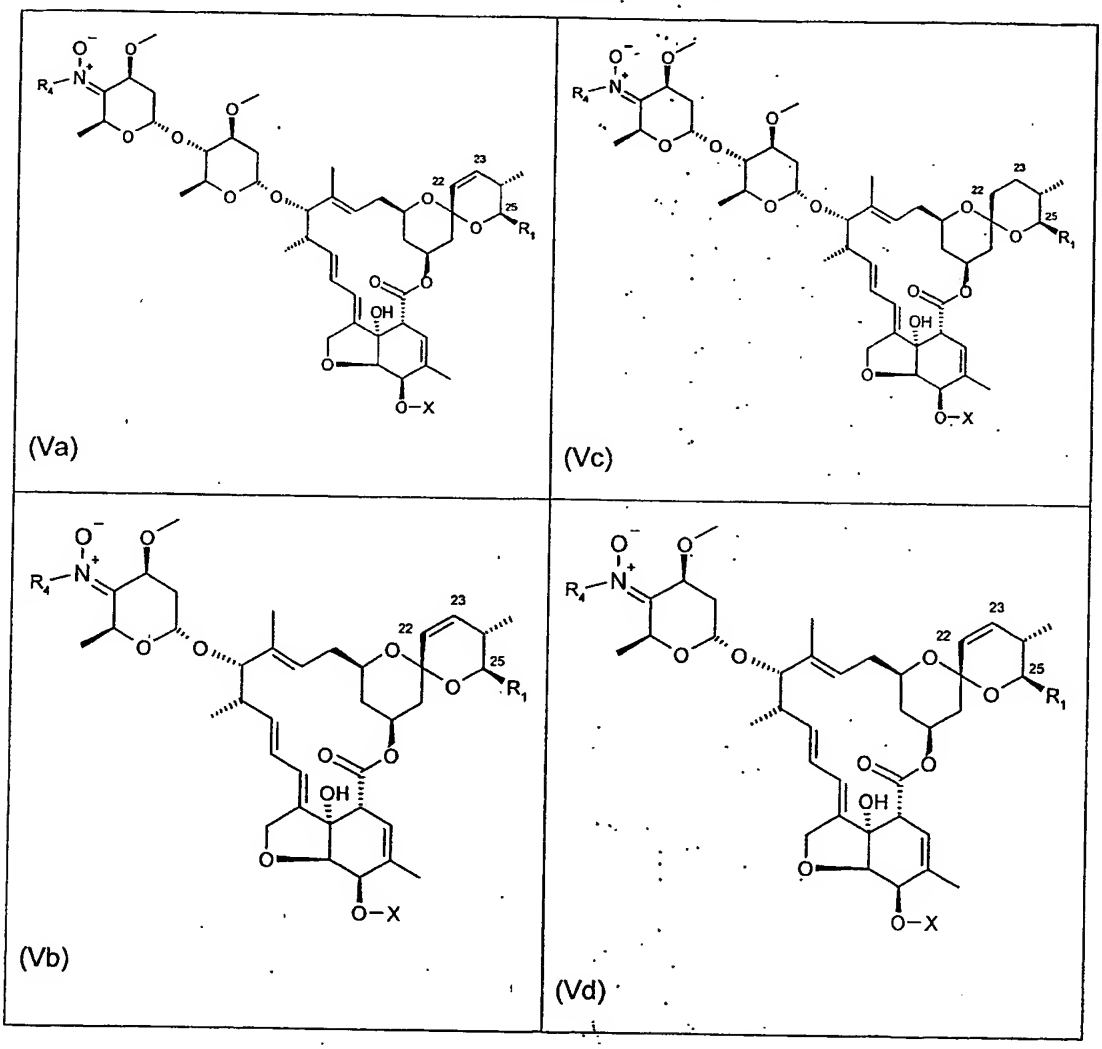
Table 49	A compound of the formula (IIIa) wherein R_1 is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 50	A compound of the formula (IIIa) wherein R_1 is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 51	A compound of the formula (IIIa) wherein R_1 is cyclohexyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the

	substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 52	A compound of the formula (IIIa) wherein R_1 is cyclohexyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 53	A compound of the formula (IIIa) wherein R_1 is 1-methyl butyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 54	A compound of the formula (IIIa) wherein R_1 is 1-methyl butyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 55	A compound of the formula (IIIb) wherein R_1 is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 56	A compound of the formula (IIIb) wherein R_1 is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 57	A compound of the formula (IIIb) wherein R_1 is cyclohexyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 58	A compound of the formula (IIIb) wherein R_1 is cyclohexyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 59	A compound of the formula (IIIb) wherein R_1 is 1-methyl butyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 60	A compound of the formula (IIIb) wherein R_1 is 1-methyl butyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 61	A compound of the formula (IIIc) wherein R_1 is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.

Table 62	A compound of the formula (IIIc) wherein R_1 is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 63	A compound of the formula (IIIc) wherein R_1 is cyclohexyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 64	A compound of the formula (IIIc) wherein R_1 is cyclohexyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 65	A compound of the formula (IIIc) wherein R_1 is 1-methyl butyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 66	A compound of the formula (IIIc) wherein R_1 is 1-methyl butyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 67	A compound of the formula (IIId) wherein R_1 is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 68	A compound of the formula (IIId) wherein R_1 is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 69	A compound of the formula (IIId) wherein R_1 is cyclohexyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 70	A compound of the formula (IIId) wherein R_1 is cyclohexyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 71	A compound of the formula (IIId) wherein R_1 is 1-methyl butyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.
Table 72	A compound of the formula (IIId) wherein R_1 is 1-methyl butyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration,

	and the substituents R_8 and Q corresponds to a line 1 to 6 of Table Y.

Table Z: A compound of any one of the formulae (Va to Vd)



where

Line	R_4	X
1	CH_3	$SitBu(CH_3)_2$

Line	R_4	X
2	CH_3	H
3	$PhCH_2$	$SitBu(CH_3)_2$
4	$PhCH_2$	H
5	$CH_2CH\ CH_2$	$SitBu(CH_3)_2$
6	$CH_2CH\ CH_2$	H
7	$CH_3\ CH_2$	$SitBu(CH_3)_2$
8	$CH_3\ CH_2$	H
9	iPr	$SitBu(CH_3)_2$
10	iPr	H
11	tBu	$SitBu(CH_3)_2$
12	tBu	H
13		$SitBu(CH_3)_2$
14		H

and

Table 73	A compound of the formula (Va) wherein R_1 is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 74	A compound of the formula (Va) wherein R_1 is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 75	A compound of the formula (Va) wherein R_1 is cyclohexyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.

Table 76	A compound of the formula (Va) wherein R_1 is cyclohexyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 77	A compound of the formula (Va) wherein R_1 is 1-methyl butyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 78	A compound of the formula (Va) wherein R_1 is 1-methyl butyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 79	A compound of the formula (Vb) wherein R_1 is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 80	A compound of the formula (Vb) wherein R_1 is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 81	A compound of the formula (Vb) wherein R_1 is cyclohexyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 82	A compound of the formula (Vb) wherein R_1 is cyclohexyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 83	A compound of the formula (Vb) wherein R_1 is 1-methyl butyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 84	A compound of the formula (Vb) wherein R_1 is 1-methyl butyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 85	A compound of the formula (Vc) wherein R_1 is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 86	A compound of the formula (Vc) wherein R_1 is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration,

	and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 87	A compound of the formula (Vc) wherein R_1-is cyclohexyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 88	A compound of the formula (Vc) wherein R_1 is cyclohexyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 89	A compound of the formula (Vc) wherein R_1 is 1-methyl butyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 90	A compound of the formula (Vc) wherein R_1 is 1-methyl butyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 91	A compound of the formula (Vd) wherein R_1 is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 92	A compound of the formula (Vd) wherein R_1 is sec-butyl or isopropyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 93	A compound of the formula (Vd) wherein R_1 is cyclohexyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 94	A compound of the formula (Vd) wherein R_1 is cyclohexyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 95	A compound of the formula (Vd) wherein R_1 is 1-methyl butyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is E configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.
Table 96	A compound of the formula (Vd) wherein R_1 is 1-methyl butyl, the bond between the carbon atom at the 4' or 4" position (as appropriate) and nitrogen atom is Z configuration, and the substituents R_4 and X corresponds to a line 1 to 14 of Table Z.

In the area of pest control, a compound of formula (I), (III) or (V) is an active compound (also referred to as active ingredient) exhibiting valuable preventive and/or curative activity with a very advantageous biocidal spectrum and a very broad spectrum, even at low rates of concentration, while being well tolerated by warm-blooded animals, fish and plants. They are, surprisingly, equally suitable for controlling both plant pests and ecto- and endo-parasites in humans and more especially in productive livestock, domestic animals and pets. They are effective against all or individual development stages of normally sensitive animal pests, but also of resistant animal pests, such as representatives of the class insecta, order Acarina, class nematoda, cestodes and trematodes, while at the same time protecting useful organisms. The insecticidal, acaricidal or nematicidal activity of the active ingredients according to the invention may manifest itself directly, *i.e.*, in the mortality of the pests, which occurs immediately or only after some time, for example during moulting, or indirectly, for example in reduced oviposition and/or hatching rate, good activity corresponding to a mortality of at least 50 to 60 %.

Successful control within the scope of the subject of the invention is possible, in particular, of pests from the orders Lepidoptera, Coleoptera, Orthoptera, Isoptera, Psocoptera, Anoplura, Mallophaga, Thysanoptera, Heteroptera, Homoptera, Hymenoptera, Diptera, Siphonaptera, Thysanura and Acarina, mainly Lepidoptera and Coleoptera. Very especially good control is possible of the following pests:

Abagrotis spp., Abraxas spp., Acantholeucania spp., Acanthoplusia spp., Acarus spp., Acarus siro, Aceria spp., Aceria sheldoni, Acleris spp.; Acoloithus spp., Acompsia spp., Acossus spp., Acria spp., Acrobasis spp., Acrocercops spp., Acrolepia spp., Acrolepiopsis spp., Acronicta spp., Acropolitis spp., Actebia spp., Aculus spp., Aculus schlechtendali, Adoxophyes spp., Adoxophyes reticulana, Aedes spp., Aegeria spp., Aethes spp., Agapeta spp., Agonopterix spp., Agriopis spp., Agriotes spp., Agriphila spp., Agrochola spp., Agroperina spp., Alabama ssp., Alabama argillaceae, Agrotis spp., Albuna spp., Alcathoe spp., Alcis spp., Aleimma spp., Aletia spp., Aleurothrixus spp., Aleurothrixus floccosus, Aleyrodes spp., Aleyrodes brassicae, Allophyes spp., Alsophila spp., Amata spp., Amathes

spp., Amblyomma spp., Amblyptilia spp., Ammoconia spp., Amorbia spp., Amphion spp., Amphipoea spp., Amphipyra spp., Amyelois spp., Anacamptodes spp., Anagrapha spp., Anarsia spp., Anatrychyntis spp., Anavitrinella spp., Ancylis spp., Andropolia spp., Anhimella spp., Antheraea spp., Antherigona spp., Antherigona soccata, Anthonomus ssp., Anthonomus grandis, Anticarsia spp., Anticarsia gemmatalis, Aonidiella spp., Apamea spp., Aphania spp., Aphelia spp., Aphididae, Aphis spp., Apotomis spp., Aproaerema spp., Archippus spp., Archips spp., Acromyrmex, Arctia spp., Argas spp., Argolamprotes spp., Argyresthia spp., Argyrogramma spp., Argyroploce spp., Argyrotaenia spp., Arotrophora spp., Ascotis spp., Aspidiotus spp., Aspilapteryx spp., Asthenoptycha spp., Aterpia spp., Athetis spp., Atomaria spp., Atomaria linearis, Atta spp., Atypha spp., Autographa spp., Axylia spp., Bactra spp., Barbara spp., Batrachedra spp., Battaristis spp., Bembecia spp., Bemisia spp., Bemisia tabaci, Bibio spp., Bibio hortulanis, Bisigna spp., Blastesthia spp., Blatta spp., Blatella spp., Blepharosis spp., Bleptina spp., Boarmia spp., Bombyx spp., Bomolocha spp., Boophilus spp., Brachmia spp., Bradina spp., Brevipalpus spp., Brithys spp., Bryobia spp., Bryobia praetiosa, Bryotropha spp., Bupalus spp., Busseola spp., Busseola fusca, Cabera spp., Cacoecimorpha spp., Cadra spp., Cadra cautella, Caenurgina spp., Calipitrimerus spp., Callierges spp., Callophpora spp., Callophpora erythrocephala, Calophasia spp., Caloptilia spp., Calybites spp., Capnoptycha spp., Capua spp., Caradrina spp., Caripeta spp., Carmenta spp., Carposina spp., Carposina nipponensis, Catamacta spp., Catelaphris spp., Catoptria spp., Caustoloma spp., Celaena spp., Celypha spp., Cenopis spp., Cephus spp., Ceramica spp., Cerapteryx spp., Ceratitis spp, Ceratophyllus spp., Ceroplaster spp., Chaetocnema spp., Chaetocnema tibialis, Chamaesphecia spp., Charanvca spp., Cheimophila spp., Chersotis spp., Chiasmia spp., Chilo spp., Chionodes spp., Chorioptes spp., Choristoneura spp., Chrysaspidia spp., Chrysodeixis spp., Chrysomya spp., Chrysomphalus spp., Chrysomphalus dictyospermi, Chrysomphalus aonidium, Chrysoteuchia spp., Cilix spp., Cimex spp., Clysia spp., Clysia ambiguella, Clepsis spp., Cnaemidophorus spp., Cnaphalocrocis spp., Cnephasia spp., Coccus spp., Coccus hesperidum, Cochylis spp., Coleophora spp., Colotois spp., Commophila spp., Conistra spp., Conopomorpha spp., Corcyra spp., Cornutiplusia spp., Cosmia spp., Cosmopolites spp., Cosmopterix spp., Cossus spp., Costaeonvexa spp., Crambus spp., Creatonotos spp., Crocidolomia spp., Crocidolomia binotalis, Croesia spp., Crymodes spp., Cryptaspasma spp., Cryptoblabes spp., Cryptocala spp., Cryptophlebia spp., Cryptophlebia leucotreta, Cryptoptila spp., Ctenopseustis spp., Cucullia spp., Curculio spp., Culex spp., Cuterebra spp., Cydia spp., Cydia pomonella, Cymbalophora spp.,

Dactylethra spp., Dacus spp., Dadica spp., Damalinea spp., Dasychira spp., Decadarchis spp., Decodes spp., Deilephila spp., Deltodes spp., Dendrolimus spp., Depressaria spp., Dermestes spp., Dermanyssus spp., Dermanyssus gallinae, Diabrotica spp., Diachrysia spp., Diaphania spp., Diarsia spp., Diasemia spp., Diatraea spp., Diceratura spp., Dichomeris spp., Dichrocrocis spp., Dichrorampha spp., Dicycla spp., Dioryctria spp., Diparopsis spp., Diparopsis castanea, Dipleurina spp., Diprion spp., Diprionidae, Discestra spp., Distantiella spp., Distantiella theobroma, Ditula spp., Diurnea spp., Doratopteryx spp., Drepana spp., Drosphila spp., Drosphila melanogaster, Dysauxes spp., Dysdercus spp., Dysstroma spp., Eana spp., Earias spp., Ecclitica spp., Ecdytolopha spp., Ecpyrrhorrhoe spp., Ectomyelois spp., Eetropis spp., Egira spp., Elasmopalpus spp., Emmelia spp., mpoasca spp., Empyreuma spp., Enargia spp., Enarmonia spp., Endopiza spp., Endothenia spp., Endotricha spp., Eoreuma spp., Eotetranychus spp., Eotetranychus carpini, Epagoge spp., Epelis spp., Ephestia spp., Ephestiodes spp., Epiblema spp., Epiehoristodes spp., Epinotia spp., Epiphyas spp., Epiplema spp., Epipsestis spp., Epirrhoe spp., Episimus spp., Epitymbia spp., Epllachna spp., Erannis spp., Erastria spp., Eremnus spp., Ereunetis spp., Eriophyes spp., Eriosoma spp., Eriosoma lanigerum, Erythroneura spp., Estigmene spp., Ethmia spp., Etiella spp., Euagrotis spp., Eucosma spp., Euehlaena spp., Euelidia spp., Eueosma spp., Euchistus spp., Eucosmomorpha spp., Eudonia spp., Eufidonia spp., Euhyponomeutoides spp., Eulepitodes spp., Eulia spp., Eulithis spp., Eupithecia spp., Euplexia spp., Eupoecilia spp., Eupoecilia ambiguella, Euproctis spp., Eupsilia spp., Eurhodope spp., Eurois spp., Eurygaster spp., Eurythmia spp., Eustrotia spp., Euxoa spp., Euzophera spp., Evergestis spp., Evippe spp., Exartema spp., Fannia spp., Faronta spp., Feltia spp., Filatima spp., Fishia spp., Frankliniella spp., Fumibotys spp., Gaesa spp., Gasgardia spp., Gastrophilus spp., Gelechia spp., Gilpinia spp., Gilpinia polytoma, Glossina spp., Glyphipterix spp., Glyphodes spp., Gnorimoschemini spp., Gonodonta spp., Gortyna spp., Gracillaria spp., Graphania spp., Grapholita spp., Grapholitha spp., Gravitarmata spp., Gretchena spp., Griselda spp., Gryllotalpa spp., Gynaephora spp., Gypsonoma spp., Hada spp., Haematopinus spp., Halisidota spp., Harpipteryx spp., Harrisina spp., Hedya spp., Helicoverpa spp., Heliophobus spp., Heliothis spp., Hellula spp., Helotropa spp., Hemaris spp., Hercinothrips spp., Herculia spp., Hermonassa spp., Heterogenea spp., Holomelina spp., Homadaula spp., Homoeosoma spp., Homoglaea spp., Homohadena spp., Homona spp., Homonopsis spp., Hoplocampa spp., Hoplodrina spp., Hoshinoa spp., Hxalomma spp., Hydraecia spp., Hydriomena spp., Hyles spp., Hyloicus spp., Hypagyrtis spp., Hypatima spp., Hyphantria spp., Hyphantria

cunea, Hypocala spp., Hypocoena spp., Hypodema spp., Hyppobosca spp., Hypsipyla spp., Hyssia spp., Hysterosia spp., Idaea spp., Idia spp., Ipimorpha spp., Isia spp., Isochorista spp., Isophrictis spp., Isopolia spp., Isotrias spp., Ixodes spp., Itame spp., Jodia spp., Jodis spp., Kawabea spp., Keiferia spp., Keiferia lycopersicella, Labdia spp., Lacinipolia spp., Lambdina spp., Lamprothritpa spp., Laodelphax spp., Lasius spp., Laspeyresia spp., Leptinotarsa spp., Leptinotarsa decemlineata, Leptocorisa spp., Leptostales spp., Lecanium spp., Lecanium comi, Lepidosaphes spp., Lepisma spp., Lepisma saccharina , Lesmone spp., Leucania spp., Leucinodes spp., Leucophaea spp., Leucophaea maderae, Leucoptera spp., Leucoptera scitella, Linognathus spp., Liposcelis spp., Lissorhoptrus spp., Lithacodia spp., Lithocolletis spp., Lithomoia spp., Lithophane spp., Lixodessa spp., Lobesia spp., Lobesia botrana, Lobophora spp., Locusta spp., Lomanaltes spp., Lomographa spp., Loxagrotis spp., Loxostege spp., Lucilia spp., Lymantria spp., Lymnaecia spp., Lyonetia spp., Lyriomyza spp., Macdonnoughia spp., Macrauzata spp., Macronoctua spp., Macrosiphus spp., Malacosoma spp., Maliarpha spp., Mamestra spp., Mamestra brassicae, Manduca spp., Manduca sexta, Marasmia spp., Margaritia spp., Matratinea spp., Matsumuraeses spp., Melanagromyza spp., Melipotes spp., Melissopus spp., Melittia spp., Melolontha spp., Meristis spp., Meritastis spp., Merophyas spp., Mesapamea spp., Mesogona spp., Mesoleuca spp., Metanema spp., Metendothenia spp., Metzneria spp., Micardia spp., Microcorses spp., Microleon spp., Mnesictena spp., Mocis spp., Monima spp., Monochroa spp., Monomorium spp., Monomorium pharaonis, Monopsis spp., Morrisonia spp., Musca spp., Mutuuraia spp., Myelois spp., Mythimna spp., Myzus spp., Naranga spp., Nedra spp., Nemapogon spp., Neodiprion spp., Neosphaleroptera spp., Nephelodes spp., Nephotettix spp., Nezara spp., Nilaparvata spp., Niphonympha spp., Nippoptilia spp., Noctua spp., Nola spp., Notocelia spp., Notodonta spp., Nudaurelia spp., Ochropleura spp., Ocnerostoma spp., Oestrus spp., Olethreutes spp., Oligia spp., Olindia spp., Olygonychus spp., Olygonychus gallinae, Oncocnemis spp., Operophtera spp., Ophisma spp., Opogona spp., Oraesia spp., Orniodoros spp., Orgyia spp., Oria spp., Orseolia spp., Orthodes spp., Orthogonia spp., Orthosia spp., Oryzaephilus spp., Oscinella spp., Oscinella frit, Osminia spp., Ostrinia spp., Ostrinia nubilalis, Otiorhynchus spp., Ourapteryx spp., Pachetra spp., Pachysphinx spp., Pagyda spp., Paleacrita spp., Paliga spp., Palthis spp., Pammene spp., Pandemis spp., Panemeria spp., Panolis spp., Panolis flammea, Panonychus spp., Parargyresthia spp., Paradiarsia spp., Paralobesia spp., Paranthrene spp., Parapandemis spp., Parapediasia spp., Parastichtis spp., Parasyndemis spp., Paratoria spp., Pareromeme spp., Pectinophora spp., Pectinophora gossypiella,

Pediculus spp., Pegomyia spp., Pegomyia hyoscyami, Pelochrista spp., Pennisetia spp., Penstemonia spp., Pemphigus spp., Peribatodes spp., Peridroma spp.; Perileucoptera spp., Periplaneta spp., Perizoma spp., Petrova spp., Pexicopia spp., Phalonia spp., Phalonidia spp., Phaneta spp., Phlyctaenia spp., Phlyctinus spp., Phorbia spp., Phragmatobia spp., Phricanthes spp., Phthorimaea spp., Phthorimaea operculella, Phyllocnistis spp., Phyllocoptruta spp., Phyllocoptruta oleivora, Phyllonorycter spp., Phyllophila spp., Phylloxera spp., Pieris spp., Pieris rapae, Piesma spp., Planococus spp., Planotortrix spp., Platyedra spp., Platynota spp., Platyptilia spp., Platysenta spp., Plodia spp., Plusia spp., Plutella spp., Plutella xylostella, Podosesia spp., Polia spp., Popillia spp., Polymixis spp., Polyphagotarsonemus spp., Polyphagotarsonemus latus, Prays spp., Prionoxystus spp., Probole spp., Proceras spp., Prochoerodes spp., Proeulia spp., Proschistis spp., Proselena spp., Proserpinus spp., Protagrotis spp., Proteoteras spp., Protobathra spp., Protoschinia spp., Pselnophorus spp., Pseudaletia spp., Pseudanthonomus spp., Pseudaternelia spp., Pseudaulacaspis spp., Pseudexentera spp., Pseudococus spp., Pseudohermenias spp., Pseudoplusia spp., Psoroptes spp., Psylla spp., Psylliodes spp., Pterophorus spp., Ptycholoma spp., Pulvinaria spp., Pulvinaria aethiopica, Pyralis spp., Pyrausta spp., Pyrgotis spp., Pyrreferra spp., Pyrrharctia spp., Quadraspidiotus spp., Rancora spp., Raphia spp., Reticulitermes spp., Retinia spp., Rhagoletis spp, Rhagoletis pomonella, Rhipicephalus spp., Rhizoglyphus spp., Rhizopertha spp., Rhodnius spp., Rhophalosiphum spp., Rhopobota spp., Rhyacia spp., Rhyacionia spp., Rhynchopacha spp., Rhyzosthenes spp., Rivula spp., Rondotia spp., Rusidrina spp., Rynchaglaea spp., Sabulodes spp., Sahlbergella spp., Sahlbergella singularis, Saissetia spp., Samia spp., Sannina spp., Sanninoidea spp., Saphoideus spp., Sarcoptes spp., Sathrobrota spp., Scarabeidae, Sceliodes spp., Schinia spp., Schistocerca spp., Schizaphis spp., Schizura spp., Schreckensteinia spp., Sciara spp., Scirpophaga spp., Scirthrips auranti, Scoparia spp., Scopula spp., Scotia spp., Scotinophara spp., Scotogramma spp., Scrobipalpa spp., Scrobipalpopsis spp., Semiothisa spp., Sereda spp., Sesamia spp., Sesia spp., Sicya spp., Sideridis spp., Simyra spp., Sineugraphe spp., Sitochroa spp., Sitobion spp., Sitophilus spp., Sitotroga spp., Solenopsis spp., Smerinthus spp., Sophronia spp., Spaelotis spp., Spargaloma spp., Sparganothis spp., Spatalistis spp., Sperchia spp., Sphecia spp., Sphinx spp., Spilonota spp., Spodoptera spp., Spodoptera littoralis, Stagmatophora spp., Staphylinochrous spp., Stathmopoda spp., Stenodes spp., Sterrha spp., Stomoxys spp., Strophedra spp., Sunira spp., Sutyna spp., Swammerdamia spp., Syllomatia spp., Sympistis spp., Synanthedon spp., Synaxis spp., Syncopacma spp.,

Syndemis spp., Syngrapha spp., Synthomeida spp., Tabanus spp., Taeniarchis spp., Taeniothrips spp., Tannia spp., Tarsonemus spp., Tegulifera spp., Tehama spp., Teleiodes spp., Telorta spp., Tenebrio spp., Tephrina spp., Teratoglaea spp., Terricula spp., Tethea spp., Tetranychus spp., Thalpophila spp., Thaumetopoea spp., Thiodia spp., Thrips spp., Thrips palmi, Thrips tabaci, Thyridopteryx spp., Thyris spp., Tineola spp., Tipula spp., Tortricidia spp., Tortrix spp., Trachea spp., Trialeurodes spp., Trialeurodes vaporariorum, Triatoma spp., Triaxomera spp., Tribolium spp., Tricodectes spp., Trichoplusia spp., Trichoplusia ni, Trichoptilus spp., Trioza spp., Trioza erytreae, Triphaenia spp., Triphosa spp., Trogoderma spp., Tyria spp., Udea spp., Unaspis spp., Unaspis citri, Utetheisa spp., Valeriodes spp., Vespa spp., Vespamima spp., Vitacea spp., Vitula spp., Witlesia spp., Xanthia spp., Xanthorhoe spp., Xanthotype spp., Xenomicta spp., Xenopsylla spp., Xenopsylla cheopsis, Xestia spp., Xylena spp., Xylomyges spp., Xyrosaris spp., Yponomeuta spp., Ypsolopha spp., Zale spp., Zanclognathus spp., Zeiraphera spp., Zenodoxus spp., Zeuzera spp., Zygaena spp.,

It is also possible to control pests of the class Nematoda using the compounds according to the invention. Such pests include, for example,

root knot nematodes, cyst-forming nematodes and also stem and leaf nematodes;

especially of Heterodera spp., *e.g.*, Heterodera schachtii, Heterodora avenae and Heterodora trifolii; Globodera spp., e.g. Globodera rostochiensis; Meloidogyne spp., *e.g.*, Meloidogyne incognita and Meloidogyne javanica; Radopholus spp., *e.g.*, Radopholus similis; Pratylenchus, *e.g.*, Pratylenchus neglectans and Pratylenchus penetrans; Tylenchulus, *e.g.*, Tylenchulus semipenetrans; Longidorus, Trichodorus, Xiphinema, Ditylenchus, Apheenchoides and Anguina; especially Meloidogyne, *e.g.*, Meloidogyne incognita, and Heterodera, *e.g.*, Heterodera glycines.

An especially important aspect of the present invention is the use of the compound of formula (I), (III) or (V) in the protection of plants against parasitic feeding pests.

The action of the compound of formula (I), (III) or (V) and the compositions comprising the said compound against animal pests can be significantly broadened and adapted to the given circumstances by the addition of other insecticides, acaricides or nematicides. Suitable additives include, for example, representatives of the following classes of active ingredient: organophosphorus compounds, nitrophenols and derivatives, formamidines, ureas, carbamates, pyrethroids, chlorinated hydrocarbons, neonicotinoids and Bacillus thuringiensis preparations.

Examples of especially suitable mixing partners include: azamethiphos; chlorfenvinphos; cypermethrin, cypermethrin high-cis; cyromazine; diafenthiuron; diazinon; dichlorvos; dicrotophos; dicyclanil; fenoxycarb; fluazuron; furathiocarb; isazofos; iodfenphos; kinoprene; lufenuron; methacriphos; methidathion; monocrotophos; phosphamidon; profenofos; diofenolan; a compound obtainable from the Bacillus thuringiensis strain GC91 or from strain NCTC11821; pymetrozine; bromopropylate; methoprene; disulfoton; quinalphos; tau-fluvalinate; thiocyclam; thiometon; aldicarb; azinphos-methyl; benfuracarb; bifenthrin; buprofezin; carbofuran; dibutylaminothio; cartap; chlorfluazuron; chlorpyrifos; cyfluthrin; lambda-cyhalothrin; alpha-cypermethrin; zeta-cypermethrin; deltamethrin; diflubenzuron; endosulfan; ethiofencarb; fenitrothion; fenobucarb; fenvalerate; formothion; methiocarb; heptenophos; imidacloprid; thiamethoxam; clothianidine; isoprocarb; methamidophos; methomyl; mevinphos; parathion; parathion-methyl; phosalone; pirimicarb; propoxur; teflubenzuron; terbufos; triazamate; fenobucarb; tebufenozide; fipronil; beta-cyfluthrin; silafluofen; fenpyroximate; pyridaben; fenazaquin; pyriproxyfen; pyrimidifen; nitenpyram; acetamiprid; abamectin; emamectin; emamectin-benzoate; spinosad; a plant extract that is active against insects; a preparation that comprises nematodes and is active against insects; a preparation obtainable from Bacillus subtilis; a preparation that comprises fungi and is active against insects; a preparation that comprises viruses and is active against insects; chlorfenapyr; acephate; acrinathrin; alanycarb; alphamethrin; amitraz; AZ 60541; azinphos A; azinphos M; azocyclotin; bendiocarb; bensultap; beta-cyfluthrin; BPMC; brofenprox; bromophos A; bufencarb; butocarboxin; butylpyridaben; cadusafos; carbaryl; carbophenothion; chloethocarb; chlorethoxyfos; chlormephos; cis-resmethrin; clocythrin; clofentezine; cyanophos; cycloprothrin; cyhexatin; demeton M; demeton S; demeton-S-methyl; dichlofenthion; dicliphos; diethion; dimethoate; dimethylvinphos; dioxathion; edifenphos; esfenvalerate; ethion; ethofenprox; ethoprophos; etrimphos; fenamiphos;

fenbutatin oxide; fenothiocarb; fenpropathrin; fenpyrad; fenthion; fluazinam; flucycloxuron; flucythrinate; flufenoxuron; flufenprox; fonophos; fosthiazate; fubfenprox; HCH; hexaflumuron; hexythiazox; IKI-220; iprobenfos; isofenphos; isoxathion; ivermectin; malathion; mecarbam; mesulfenphos; metaldehyde; metolcarb; milbemectin; moxidectin; naled; NC 184; omethoate; oxamyl; oxydemethon M; oxydeprofos; permethrin; phenthoate; phorate; phosmet; phoxim; pirimiphos M; pirimiphos E; promecarb; propaphos; prothiofos; prothoate; pyrachlophos; pyradaphenthion; pyresmethrin; pyrethrum; tebufenozide; salithion; sebufos; sulfotep; sulprofos; tebufenpyrad; tebupirimphos; tefluthrin; temephos; terbam; tetrachlorvinphos; thiacloprid; thiafenox; thiodicarb; thiofanox; thionazin; thuringiensin; tralomethrin; triarthene; triazophos; triazuron; trichlorfon; triflumuron; trimethacarb; vamidothion; xylylcarb; YI 5301/5302; zetamethrin; DPX-MP062 — indoxacarb; methoxyfenozide; bifenazate; XMC (3,5-xylyl methylcarbamate); or the fungus pathogen Metarhizium anisopliae.

A compound of formula (I), (III) or (V) can be used to control, *i.e.*, to inhibit or destroy, pests of the mentioned type occurring on plants, especially on useful plants and ornamentals in agriculture, in horticulture and in forestry, or on parts of such plants, such as the fruits, blossoms, leaves, stems, tubers or roots, while in some cases plant parts that grow later are still protected against those pests.

Target crops include especially cereals, such as wheat, barley, rye, oats, rice, maize and sorghum; beet, such as sugar beet and fodder beet; fruit, *e.g.*, pomes, stone fruit and soft fruit, such as apples, pears, plums, peaches, almonds, cherries and berries, *e.g.*, strawberries, raspberries and blackberries; leguminous plants, such as beans, lentils, peas and soybeans; oil plants, such as rape, mustard, poppy, olives, sunflowers, coconut, castor oil, cocoa and groundnuts; cucurbitaceae, such as marrows, cucumbers and melons; fibre plants, such as cotton, flax, hemp and jute; citrus fruits, such as oranges, lemons, grapefruit and mandarins; vegetables, such as spinach, lettuce, asparagus, cabbages, carrots, onions, tomatoes, potatoes and paprika; lauraceae, such as avocado, cinnamon and camphor; and tobacco, nuts, coffee, aubergines, sugar cane, tea, pepper, vines, hops, bananas, natural rubber plants and ornamentals.

Further areas of use of a compound of formula (I), (III) or (V) is the protection of stored goods and storerooms and the protection of raw materials, and also in the hygiene sector, especially the protection of domestic animals and productive livestock against pests of the mentioned type, more especially the protection of domestic animals, especially cats and dogs, from infestation by fleas, ticks and nematodes.

The invention therefore relates also to a pesticidal composition, such as emulsifiable concentrates, suspension concentrates, directly sprayable or dilutable solutions, spreadable pastes, dilute emulsions, wettable powders, soluble powders, dispersible powders, wettable powders, dusts, granules and encapsulations of polymer substances, that comprises at least one compound of formula (I), (III) or (V), the choice of formulation being made in accordance with the intended objectives and the prevailing circumstances. Furthermore, the pesticidal composition is often diluted, and optionally combined with other pesticidal compositions, before its use as a pesticide. The invention, therefore, also relates to a tank mix composition (sometimes referred to as a slurry in the event the composition is a suspension), which comprises the pesticidal composition and a liquid carrier, generally water, and optionally one or more other pesticidal compositions, each other pesticidal composition comprising a further pesticide as active compound.

The active ingredient is used in those compositions in pure form, a solid active ingredient, for example, in a specific particle size, or preferably together with at least one of the auxiliary (also known as adjuvants) customary in formulation technology, such as extenders, *e.g.*, solvents or solid carriers, or surface-active compounds (surfactants). In the area of parasite control in humans, domestic animals, productive livestock and pets it will be self-evident that only physiologically tolerable additives are used.

Solvents are, for example: non-hydrogenated or partly hydrogenated aromatic hydrocarbons, preferably fractions C_8 to C_{12} of alkylbenzenes, such as xylene mixtures, alkylated naphthalenes or tetrahydronaphthalene, aliphatic or cycloaliphatic hydrocarbons,

such as paraffins or cyclohexane, alcohols, such as ethanol, propanol or butanol, glycols and ethers and esters thereof, such as propylene glycol, dipropylene glycol ether, ethylene glycol or ethylene glycol monomethyl or -ethyl ether, ketones, such as cyclohexanone, isophorone or diacetone alcohol, strongly polar solvents, such as N-methylpyrrolid-2-one, dimethyl sulfoxide or N,N-dimethylformamide, water, non-epoxidized or epoxidized plant oils, such as non-epoxidized or epoxidized rapeseed, castor, coconut or soya oil, and silicone oils.

The solid carriers used, for example, for dusts and dispersible powders, are as a rule natural rock powders, such as calcite, talc, kaolin, montmorillonite or attapulgite. Highly disperse silicic acids or highly disperse absorbent polymers can also be added to improve the physical properties. Granular adsorptive granule carriers are porous types, such as pumice, crushed brick, sepiolite or bentonite, and non-sorbent carrier materials are calcite or sand. A large number of granular materials of inorganic or organic nature can furthermore be used, in particular dolomite or comminuted plant residues.

Surface-active compounds are, depending on the nature of the active compound to be formulated, nonionic, cationic and/or anionic surfactants or surfactant mixtures with good emulsifying, dispersing and wetting properties. The surfactants listed below are to be regarded only as examples; many other surfactants that are customary in formulation technology are suitable and are described in the relevant literature.

Nonionic surfactants are, in particular, polyglycol ether derivatives of aliphatic or cycloaliphatic alcohols, saturated or unsaturated fatty acids and alkylphenols, which can contain 3 to 30 glycol ether groups and 8 to 20 carbon atoms in the (aliphatic) hydrocarbon radical and 6 to 18 carbon atoms in the alkyl radical of the alkylphenols. Substances which are furthermore suitable are water-soluble polyethylene oxide adducts, containing 20 to 250 ethylene glycol ether and 10 to 100 propylene glycol ether groups, on propylene glycol, ethylene diaminopolypropylene glycol and alkyl polypropylene glycol having 1 to 10 carbon atoms in the alkyl chain. The compounds mentioned usually contain 1 to 5 ethylene glycol units per propylene glycol unit. Examples are nonylphenol-polyethoxyethanols, castor oil

polyglycol ethers, polypropylene-polyethylene oxide adducts, tributylphenoxypoly-ethoxyethanol, polyethylene glycol and octylphenoxypolyethoxyethanol. Other substances are fatty acid esters of polyoxyethylene sorbitan, such as polyoxyethylene sorbitan trioleate.

The cationic surfactants are, in particular, quaternary ammonium salts which contain, as substituents, at least one alkyl radical having 8 to 22 C atoms and, as further substituents, lower, non-halogenated or halogenated alkyl, benzyl or lower hydroxyalkyl radicals. The salts are preferably in the form of halides, methyl-sulfates or ethyl-sulfates. Examples are stearyl-trimethyl-ammonium chloride and benzyl-di-(2-chloroethyl)-ethyl-ammonium bromide.

Suitable anionic surfactants can be both water-soluble soaps and water-soluble synthetic surface-active compounds. Suitable soaps are the alkali metal, alkaline earth metal and substituted or unsubstituted ammonium salts of higher fatty acids (C_{10}-C_{22}), such as the sodium or potassium salts of oleic or stearic acid, or of naturally occurring fatty acid mixtures, which can be obtained, for example, from coconut oil or tall oil; and furthermore also the fatty acid methyl-taurine salts. However, synthetic surfactants are more frequently used, in particular fatty sulfonates, fatty sulfates, sulfonated benzimidazole derivatives or alkylarylsulfonates. The fatty sulfonates and sulfates are as a rule in the form of alkali metal, alkaline earth metal or substituted or unsubstituted ammonium salts and in general have an alkyl radical of 8 to 22 C atoms, alkyl also including the alkyl moiety of acyl radicals; examples are the sodium or calcium salt of ligninsulfonic acid, of dodecylsulfuric acid ester or of a fatty alcohol sulfate mixture prepared from naturally occurring fatty acids. These also include the salts of sulfuric acid esters and sulfonic acids of fatty alcohol-ethylene oxide adducts. The sulfonated benzimidazole derivatives preferably contain 2 sulfonic acid groups and a fatty acid radical having about 8 to 22 C atoms. Alkylarylsulfonates are, for example, the sodium, calcium or triethanolammonium salts of dodecylbenzenesulfonic acid, of dibutylnaphthalenesulfonic acid or of a naphthalenesulfonic acid-formaldehyde condensation product. Corresponding phosphates, such as salts of the phosphoric acid ester of a p-nonylphenol-(4-14)-ethylene oxide adduct or phospholipids, can further also be used.

The compositions as a rule comprise 0.1 to 99 %, in particular 0.1 to 95 %, of active compound and 1 to 99.9 %, in particular 5 to 99.9 %, of at least one solid or liquid auxiliary, it being possible as a rule for 0 to 25 %, in particular 0.1 to 20 %, of the composition to be surfactants (% is in each case per cent by weight). While concentrated compositions are more preferred as commercial goods, the end user as a rule uses dilute compositions which comprise considerably lower concentrations of active compound. Preferred compositions are composed, in particular, as follows (% = per cent by weight):

Emulsifiable concentrates:

active ingredient:	1 to 90%, preferably 5 to 20%
surfactant:	1 to 30%, preferably 10 to 20%
solvent:	balance

Dusts:

active ingredient:	0.1 to 10%, preferably 0.1 to 1%
solid carrier:	99.9 to 90%, preferably 99.9 to 99%

Suspension concentrates:

active ingredient:	5 to 75%, preferably 10 to 50%
surfactant:	1 to 40%, preferably 2 to 30%
water:	balance

Wettable powders:

active ingredient: 0.5 to 90%, preferably 1 to 80%

surfactant: 0.5 to 20%, preferably 1 to 15%

solid carrier: balance

Granules:

active ingredient: 0.5 to 30%, preferably 3 to 15%

solid carrier: 99.5 to 70%, preferably 97 to 85%

Specific formulation examples for use in crop protection are given below (% = per cent by weight):

Example F1: Emulsifiable concentrates

	a)	b)	c)
Active compound	25%	40%	50%
Calcium dodecylbenzenesulphonate	5%	8%	6%
Castor oil polyethylene glycol ether (36 mol of EO)	5%	-	-
Tributylphenol polyethylene glycol ether (30 mol of EO)	-	12%	4%
Cyclohexanone	-	15%	20%
Xylene mixture	65%	25%	20%

Mixing of finely ground active compound and additives gives an emulsion concentrate which, by dilution with water, affords emulsions of the desired concentration.

Example F2: Solutions

	a)	b)	c)	d)
Active compound	80%	10%	5%	95%
Ethylene glycol monomethyl ether	-	20%	-	-
Polyethylene glycol (MW 400)	-	70%	-	-
N-methylpyrrolid-2-one	20%	-	-	-
Epoxidized coconut oil	-	-	1%	-
Aliphatic hydrocarbon (boiling range: 160-190°)	-	-	94%	5%

Mixing of finely ground active compound and additives gives a solution suitable for use in the form of microdrops.

Example F3: Granules

	a)	b)	c)	d)
Active compound	5%	10%	8%	21%
Kaolin	94%	-	79%	54%
Finely divided silicic acid	1%	-	13%	7%
Attapulgite	-	90%	-	18%

The active compound is dissolved in dichloromethane, the solution is sprayed onto the mixture of carriers and the solvent is evaporated under reduced pressure.

Example F4: Wettable powder

	a)	b)	c)
Active compound	25%	50%	75%
Sodium lignosulphonate	5%	5%	-
Sodium lauryl sulphate	3%	-	5%
Sodium diisobutylnaphthalene sulphonate	-	6%	10%
Octylphenol polyethylene glycol ether (7-8 mol of EO)	-	2%	-
Finely divided silicic acid	5%	10%	10%
Kaolin	62%	27%	-

Active compound and additives are mixed and the mixture is ground in a suitable mill. This gives wettable powders which can be diluted with water to give suspensions of the desired concentration.

Example F5: Emulsifiable concentrate

Active compound	10%
Octylphenol polyethylene glycol ether (4-5 mol of EO)	3%
Calcium dodecylbenzenesulphonate	3%
Castor oil polyethylene glycol ether (36 mol of EO)	4%
Cyclohexanone	30%
Xylene mixture	50%

Mixing of finely ground active compound and additives gives an emulsion concentrate which, by dilution with water, affords emulsions of the desired concentration.

Example F6: Extruder granules

Active compound	10%
Sodium lignosulphonate	2%
Carboxymethylcellulose	1%
Kaolin	87%

Active compound and additives are mixed, the mixture is ground, moistened with water, extruded and granulated, and the granules are dried in a stream of air.

Example F7: Coated granules

Active compound	3%
Polyethylene glycol (MW 200)	3%
Kaolin	94%

In a mixer, the finely ground active compound is applied uniformly to the kaolin which has been moistened with polyethylene glycol. This gives dust-free coated granules.

Example F8: Suspension concentrate

Active compound	40%
Ethylene glycol	10%
Nonylphenol polyethylene glycol ether (15 mol of EO)	6%
Sodium lignosulphonate	10%
Carboxymethylcellulose	1%
Aqueous formaldehyde solution (37%)	0.2%
Aqueous silicone oil emulsion (75%)	0.8%
Water	32%

Mixing of finely ground active compound and additives gives a suspension concentrate which, by dilution with water, affords suspensions of the desired concentration.

The compositions according to the invention may also comprise further solid or liquid adjuvants, such as stabilisers, *e.g.*, vegetable oils or epoxidised vegetable oils (*e.g.*, epoxidised coconut oil, rapeseed oil or soybean oil), antifoams, e.g. silicone oil, preservatives, viscosity regulators, binders and/or tackifiers as well as fertilisers or other active ingredients for obtaining special effects, *e.g.*, acaricides, bactericides, fungicides, nematicides, molluscicides or selective herbicides.

The pesticidal composition according to the invention, particularly for use as a crop protection product, is prepared in the absence of adjuvants, *e.g.*, by grinding, sieving and/or compressing the compound of formula (I), (III) or (V) (as active ingredient) or mixture thereof, for example, to a certain particle size, and in the presence of at least one adjuvant, for example, by intimately mixing and/or grinding the compound of formula (I), (III) or (V) (as active ingredient) or mixture thereof with the adjuvant(s). The invention relates likewise to those processes for the preparation of the pesticidal composition according to the invention and to the use of a compound of formula (I), (III) or (V) in the preparation of the composition.

The invention relates also to the methods of application of the pesticidal and tank mix compositions, *i.e.*, the methods of controlling pests of the mentioned type, such as spraying, atomising, dusting, coating, dressing, scattering or pouring, which are selected in accordance with the intended objectives and the prevailing circumstances, and to the use of the compositions for controlling pests of the mentioned type. Typical rates of concentration are from 0.1 to 1000 ppm, preferably from 0.1 to 500 ppm, of active ingredient. The rates of application per hectare are generally from 1 to 2000 g of active ingredient per hectare, especially from 10 to 1000 g/ha, preferably from 20 to 600 g/ha, most preferably from 20 to 100 g/ha.

A preferred method of application in the area of crop protection is application to the foliage of the plants (foliar application), the frequency and the rate of application being dependent upon the risk of infestation by the pest in question. However, the active ingredient can also penetrate the plants through the roots (systemic action) when the locus of the plants is

impregnated with a liquid formulation or when the active ingredient is incorporated in solid form into the locus of the plants, for example, into the soil, *e.g.*, in granular form (soil application). In the case of paddy rice crops, such granules may be applied in metered amounts to the flooded rice field.

The pesticidal and tank mix compositions are also suitable for protecting plant propagation material, *e.g.*, seed, such as fruits, tubers or grains, or plant cuttings, against animal pests. The propagation material can be treated with the composition before planting: seed, for example, can be dressed before being sown. The active ingredients according to the invention can also be applied to grains (coating), either by impregnating the seeds in a liquid formulation or by coating them with a solid formulation. The composition can also be applied to the planting site when the propagation material is being planted, for example, to the seed furrow during sowing. The invention relates also to such methods of treating plant propagation material and to the plant propagation material so treated.

Preparation Examples:

Since in most cases the compounds are present as mixtures of the avermectin derivatives B1a and B1b, characterization by customary physical data such as melting point or refractive index makes little sense. For this reason, the compounds are characterized by the retention times that are determined in an analysis by HPLC (high performance liquid chromatography). Here, the term B1a refers to the main component in which the group at position 25 (R_1 in formula (I)) is sec-butyl, with a content of usually more than 80%. B1b denotes the minor component in which R_1 is isopropyl. The compounds where two retention times are given both for the B1a and for the B1b derivative are mixtures of diastereoisomers, which can be separated chromatographically. In the case of compounds where a retention time is given only in column B1a or only in column B1b, the pure B1a or B1b component, respectively, can be obtained during work-up. The correct structures of the B1a and B1b components are assigned by mass spectrometry.

The following methods are used for HPLC analysis:

Method A (Water Alliance HT 2795)

HPLC gradient conditions			
Solvent A:	0.01% of acid formic in H_2O / CH_3CN (1 : 1)		
Solvent B:	0.01% of acid formic in CH_3CN		
Time [min]	A [%]	B [%]	Flow rate [ml/min]
0	100	0	1.7
2.5	0	100	1.7
2.8	0	100	1.7
2.9	100	0	1.7
Type of column	Water atlantis dc18		
Column length	20 mm		
Internal diameter of column:	3 mm		
Particle Size:	3 micron		
Temperature	40°C		

Method Z (Agilent HP1100)

HPLC gradient conditions			
Solvent A:	0.01% of trifluoroacetic acid in H_2O		
Solvent B:	0.01% of trifluoroacetic acid in CH_3CN		
Time [min]	A [%]	B [%]	Flow rate [ml/min]
0	80	20	0.5
0.1	70	30	0.5
10	40	60	0.5
14	0	100	0.5
17	0	100	0.5
17.1	80	20	0.5
22	80	20	0.5
Type of column	Zorbax Bonus-RP		
Column length	50 mm		
Internal diameter of column:	2.1 mm		

Particle Size:	3.5 micron
Temperature	40°C

Method Y (Agilent HP1100)

HPLC gradient conditions			
Solvent A:	0.01% of trifluoroacetic acid in H_2O		
Solvent B:	0.01% of trifluoroacetic acid in CH_3CN		
Time [min]	A [%]	B [%]	Flow rate [ml/min]
0	80	20	0.5
0.1	60	40	0.5
6	40	60	0.5
11	15	85	0.5
15	15	85	0.5
17	0	100	0.5
20	0	100	0.5
20.1	80	20	0.5
25	80	20	0.5
Type of column	Zorbax Bonus-RP		
Column length	50 mm		
Internal diameter of column:	2.1 mm		
Particle Size:	3.5 micron		
Temperature	40°C		

Method X (Waters Alliance 2690)

HPLC gradient conditions			
Solvent A:	0.01% of trifluoroacetic acid in H_2O		
Solvent B:	0.01% of trifluoroacetic acid in CH_3CN		
Time [min]	A [%]	B [%]	Flow rate [ml/min]
0	80	20	0.5
0.1	70	30	0.5
10	40	60	0.5

14	0	100	0.5
17	0	100	0.5
17.1	80	20	0.5
22	80	20	0.5
Type of column	Zorbax Bonus-RP		
Column length	50 mm		
Internal diameter of column:	2.1 mm		
Particle Size:	3.5 micron		
Temperature	40°C		

Method W (Waters Alliance 2690)

HPLC gradient conditions			
Solvent A:	0.01% of trifluoroacetic acid in H_2O		
Solvent B:	0.01% of trifluoroacetic acid in CH_3CN		
Time [min]	A [%]	B [%]	Flow rate [ml/min]
0	80	20	0.5
0.1	50	50	0.5
10	5	95	0.5
14	0	100	0.5
17	0	100	0.5
17.1	80	20	0.5
22	80	20	0.5
Type of column	YMC-Pack ODS-AQ		
Column length	125 mm		
Internal diameter of column:	2.0 mm		
Particle Size:	5 micron		
Temperature	40°C		

Method V (Waters Alliance 2690)

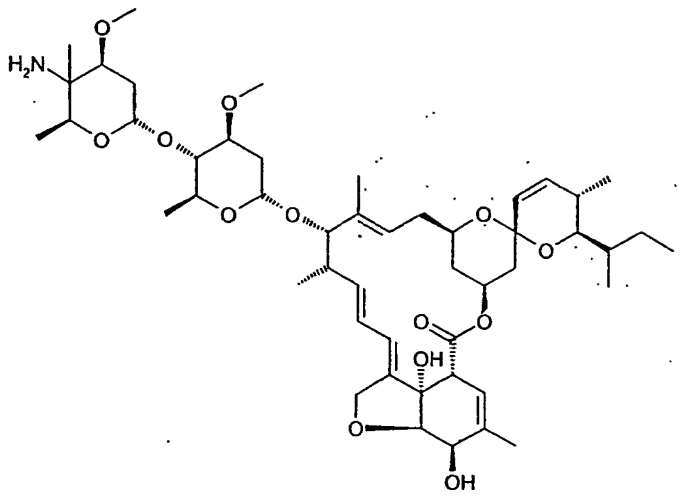
HPLC gradient conditions	
Solvent A:	0.01% of trifluoroacetic acid in H_2O

Solvent B:	0.01% of trifluoroacetic acid in CH_3CN		
Time [min]	A [%]	B [%]	Flow rate [ml/min]
0	80	20	0.5
0.1	70	30	0.5
10	40	60	0.5
14	0	100	0.5
17	0	100	0.5
17.1	80	20	0.5
22	80	20	0.5
Type of column	YMC-Pack ODS-AQ		
Column length	125 mm		
Internal diameter of column:	2.0 mm		
Particle Size:	5 micron		
Temperature	40°C		

The particular method used for HPLC analysis is indicated in the column headed "LC-MS" in Tables A to L by the letters A, Z, Y, X, W and V, as appropriate.

In the following examples, the mixing ratios of the eluents are given as volume/volume, and the temperatures in °C. Further, for simplicity, representation of the formula in the examples indicates the main derivative (B1a). TBDMS means *tert*-butyldimethysilyl.

Example P1: 4"-(R)-4"-desoxy-4"- amino-4"-methyl Avermectin B_1 and 4"-(S)-4"-desoxy-4"-amino-4"-methyl Avermectin B_1



Step A: To a solution of 40 g of 5-OTBDMS-4"-desoxy-4"-hydroxyimino-avermectin B1 and 20.3 g of diphenyl disulfide in 400 ml tetrahydrofuran at 0°C is added 23 ml of tributylphosphine. The mixture is stirred at 0°C for 1 hour. To the reaction mixture is added 80g of N-phenylmaleimide and the mixture is stirred at room temperature for 1 hour. The mixture is poured into a saturated solution of sodium hydrogencarbonate, extracted with dichloromethane, dried over Na_2SO_4, and concentrated *in vacuo*. The residue is purified by chromatography on silica gel with hexane/diethyl ether to afford 5-OTBDMS-4"-desoxy-4"-phenylsulfenimine-Avermectin B_1.

Step B: To a solution of 20 g 5-OTBDMS-4"-desoxy-4"-phenylsulfenimine-Avermectin B_1 (obtained in step A) in a mixture of 300 ml chloroform and 100 ml of saturated solution of sodium hydrogencarbonate at 0°C is added 5.9 g of m-chloroperbenzoic acid, and the mixture is stirred at 0°C for 45 minutes, poured into a aqueous saturated sodium hydrogencarbonate, extracted with dichloromethane; the organic phase is dried over sodium sulfate, and concentrated *in vacuo* to afford 5-OTBDMS-4"-desoxy--4"-phenylsulfinimine-Avermectin B_1.

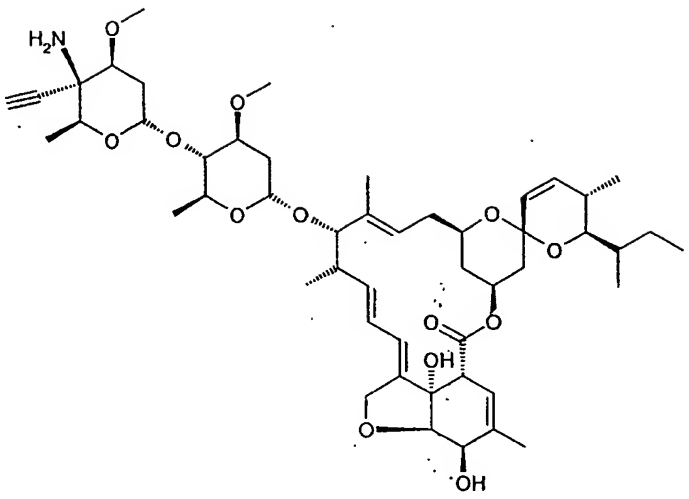
Step C: To a solution of 5-OTBDMS-4"-desoxy-4"-phenylsulfinimine-Avermectin B_1 (obtained in step B) in 360 ml of diethylether at 0°C is added 16.2 ml of methylmagnesium chloride (3M) and the mixture is stirred at O°C for 30 minutes, then the ice bath is removed. 4 ml of methylmagnesium chloride (3M) is added to the solution at RT, and the mixture is

stirred at room temperature for 10 minutes, poured into a saturated sodium chloride, extracted with ethylacetate; the organic phase is dried over sodium sulfate, and concentrated *in vacuo* to afford a mixture of 5-OTBDMS-4"-desoxy-4"-phenylsulfinamide-4"-methyl-Avermectin B_1.

Step D: To a solution of 1.2 g 5-OTBDMS-4"-desoxy-4"-phenylsulfinamide-4"-methyl-Avermectin B1 (obtained in step C) in 65 ml of dichloromethane at 0°C is added 0.46 ml of isopropanol and 0.46 ml of trifluoroacetic acid and the mixture is stirred at O°C for 1 hour, poured into a mixture of saturated sodium hydrogencarbonate and brine (1:1), extracted with ethylacetate; the organic phase is dried over sodium sulfate, and concentrated *in vacuo* to afford a mixture of 5-OTBDMS-4"-desoxy-4"-amino-4"-methyl-Avermectin B_1. The residue is purified by chromatography on silica gel with hexane/ethylacetate to afford 5-OTBDMS-4"-*(S)* -4"-desoxy-4"-amino-4"-methyl-Avermectin B_1 and 5-OTBDMS-4"-*(R)*- 4"-desoxy-4"-amino-4"-methyl-Avermectin B_1.

Step E: 0.691 g of 5-OTBDMS-4"-*(S)* -4"-desoxy-4"-amino-4"-methyl-Avermectin B_1 or 5-OTBDMS-4"-*(R)*- 4"-desoxy-4"-amino-4"-methyl-Avermectin B_1 are dissolved in 17.5 ml tetrahydrofuran, then 3.5 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into water, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with dichloromethane/methanol, yielding 4"-*(S)*- 4"-desoxy-4"-amino-4"-methyl-Avermectin B_1 or 4"-*(R)*- 4"-desoxy-4"-amino-4"-methyl-Avermectin B_1.

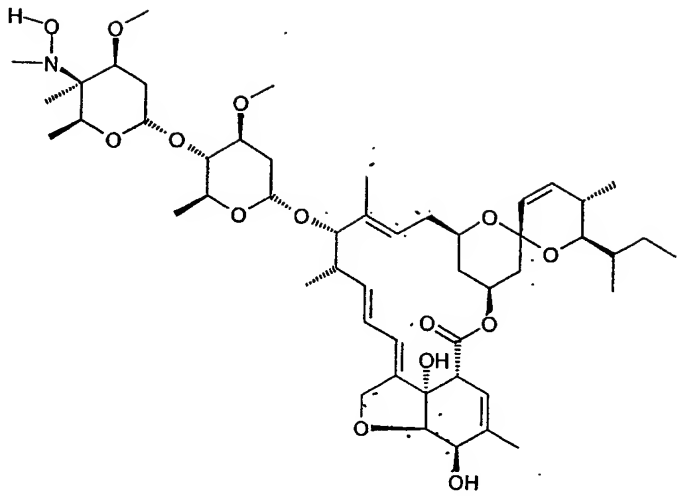
Example P2: 4"-*(R)*- 4"-desoxy-4"-amino-4"-ethynyl-Avermectin B_1



Step A: To a solution of 5-OTBDMS-4"-desoxy-4"-phenylsulfinimine-Avermectin B_1 (P1: Steps A and B) in 210 ml of tetrahydrofuran at -78°C is added 10.8 ml of trimethylsilylethynyl lithium salt (prepared in THF by action of butyllithium on trimethylsillylacetylen) and the mixture is stirred at -78°C for 20 minutes, poured into a mixture of saturated sodium chloride and ethylacetate, extracted with ethylacetate; the organic phase is dried over sodium sulfate, and concentrated *in vacuo* to afford a mixture of 5-OTBDMS-4"-*(R)*- 4"-desoxy-4"-phenylsulfinamide-4"-trimethylsilylethynyl-Avermectin B_1.

Step B: 5-OTBDMS-4"-*(R)*- 4"-desoxy-4"-phenylsulfinamide-4"-trimethylsilylethynyl-Avermectin B_1 (obtained from the step (A)) in methanol (60 ml) at 0 °C is added methanesulphonic acid (3 ml). The reaction mixture is stirred for 1hour and poured into saturated sodium bicarbonate, extracted with ethylacetate, dried over Mg_2SO_4, and concentrated *in vacuo*. Flash chromatography (silica gel, hexane/ethylacetate 1/1) affords 4"- *(R)*- 4"-desoxy-4"-amino-4"-ethynyl-Avermectin B.

Example P3: 4"-*(R)*- 4"-desoxy -4"-N-methyl hydroxylamino-4"-methyl -Avermectin B_1



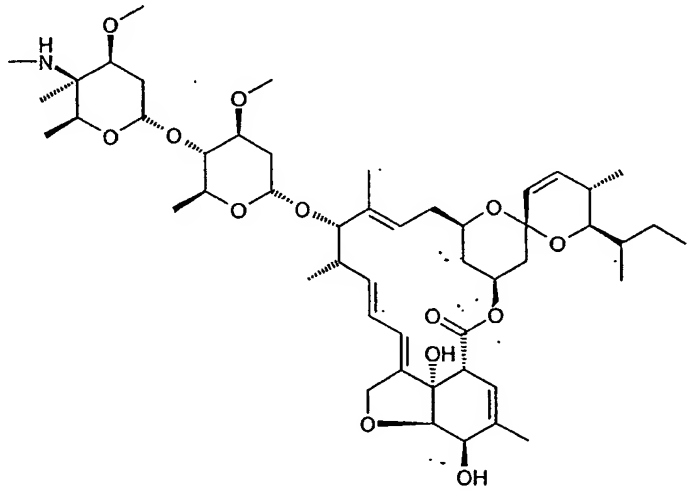
Step A: 51.86 g 5-OTBDMS-4"-desoxy-4"-oxo-avermectin B1 are dissolved in 200 ml methanol, 13.1 ml pyridine and 13.19 g N-methylhydroxylamine hydrochlorid are added. The mixture is stirred at room temperature for 5 hours, poured into sodium hydrogencarbonate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with methanol/ethylacetate, yielding 5-OTBDMS-4"-desoxy-4"- methyloxidoimino-Avermectin B_1.

Step B: To a solution of 1g of 5-OTBDMS-4"-desoxy-4"-methyloxidoimino -Avermectin B_1 (obtained in step A) in 15 ml of tetrahydrofuran at 0°C is added 0.98 ml of methylmagnesium chloride (3M) and the mixture is stirred at O°C for 30 minutes, then the ice bath is removed. 0.45 ml of methylmagnesium chloride (3M) is added to the solution at RT, and the mixture is stirred at room temperature for 10 minutes, poured into a saturated sodium chloride, extracted with ethylacetate; the organic phase is dried over sodium sulfate, and concentrated *in vacuo* The residue is purified by chromatography on silica gel with methanol/ethylacetate, yielding 5-OTBDMS-4"-*(R)*- 4"-desoxy -4"-N-methyl hydroxylamino-4"-methyl -Avermectin B_1.

Step C: 0.300 g of 5-OTBDMS-4"-*(R)*- 4"-desoxy -4"-N-methyl hydroxylamino-4"-methyl - Avermectin B_1 are dissolved in 7.5 ml tetrahydrofuran, then 3 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into water, and

extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4"-*(R)*- 4"-desoxy -4"-N-methyl hydroxylamino-4"-methyl -Avermectin B_1.

Example P4: 4"-*(R)*- 4"-desoxy-4"-methyl-4"-N-methylamino-Avermectin B_1

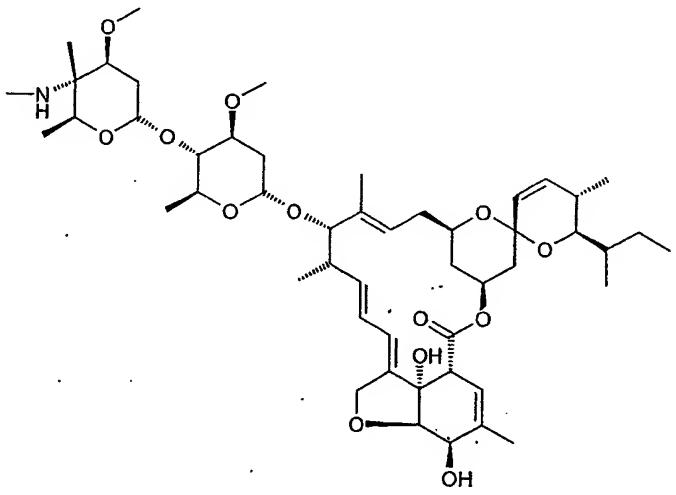


Step A : 10.85g of 5-OTBDMS-4"-*(R)*- 4"-desoxy -4"-N-methyl hydroxylamino-4"-methyl - Avermectin B_1 (P3: Steps A and B) are dissolved in 360 ml of a mixture of acetonitrile / water (3 :1), then 8.08 g of molybdenumhexacarbonyl are added. The mixture is stirred at room temperature for 6 hours, poured into sodium hydrogencarbonate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 5-OTBDMS-4"-*(R)*- 4"-desoxy -4"-N-methylamine -4"-methyl -Avermectin B_1 and 5-OTBDMS-4"-*(R)*- 4"-desoxy-4"-amino-4"-methyl-Avermectin B_1.

Step B: 0.210 g of 5-OTBDMS-4"-*(R)*- 4"-desoxy -4"-N-methylamine-4"-methyl -Avermectin B1 are dissolved in 5 ml tetrahydrofuran, then 1 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a solution of sodium

hydrogencarbonate and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with methanol/ethylacetate, yielding 4"-*(R)*- 4"-desoxy -4"-N-methylamine-4"-methyl -Avermectin B1.

Example P5: 4"-*(S)*- 4"-desoxy -4"-N-Methylamino-4"-methyl -Avermectin B_1

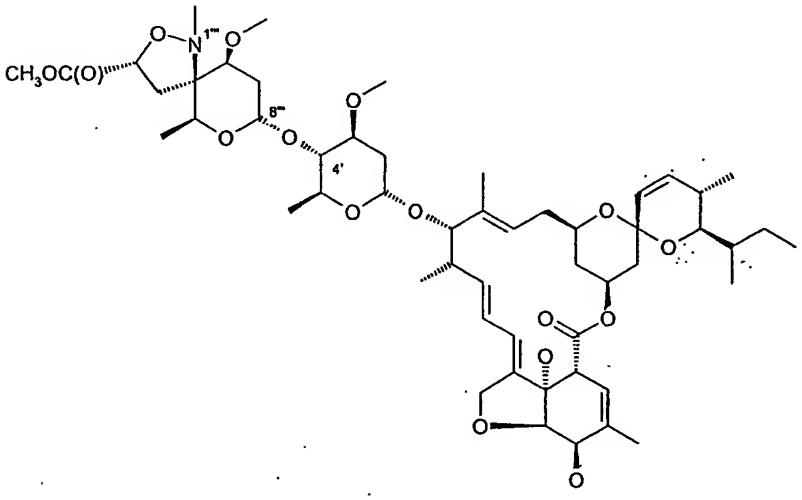


Step A: To 11.09 g of 5-OTBDMS-4"-desoxy -4"-phenylsulfinimine-Avermectin B_1 (P1: Steps A and B) in 150 ml of tetrahydrofuran at 0°C is added 11 ml of methylmagnesium chloride (3M) and the mixture is stirred at O°C for 30 minutes; then the ice bath is removed. Then 10 ml of methyliodine is added to the solution at RT, and the mixture is stirred at room temperature for 24 hours, poured into a saturated sodium chloride, extracted with ethylacetate; the organic phase is dried over sodium sulfate, and concentrated *in vacuo*. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 5-OTBDMS-4"-*(S)*- 4"-desoxy -4"-(N-phenylsulfoxid-N-methyl)amino-4"-methyl-Avermectin B_1.

Step B: 0.120 g of 5-OTBDMS-4"-*(S)*- 4"-desoxy -4"-(N-phenylsulfoxid-N-methyl)amino-4"-methyl-Avermectin B_1 are dissolved in 3 ml tetrahydrofuran, then 0.6 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridin, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a solution of sodium hydrogencarbonate and extracted with ethylacetate. Then the phases are

separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with methanol/ethylacetate, yielding 4"-*(S)*- 4"-desoxy -4"-N-methylamino-4"-methyl -Avermectin B_1.

Example P6: 4'-O-[(3'''R,5'''R,6'''S,8'''S,10'''S)-10'''-methoxy--3'''-methoxycarbonyl-1''',6'''-dimethyl-2''',7'''-dioxa-1'''-aza-spiro[4.5]deca-8'''-yl]-avermectin B1 monosaccharide

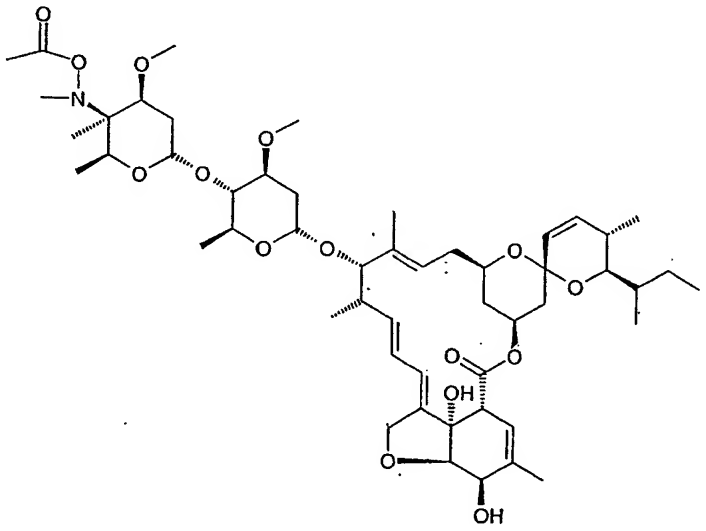


Step A : 0.5 g of 5-OTBDMS-4"-desoxy-4"- methyloxidoimino-Avermectin B_1 (P3: Step A) are dissolved in 5 ml of toluene, 0.16 ml of acrylic acid methyl ester is added. The mixture is stirred at room temperature for 24 hours, poured on silica gel and eluted with hexane/ethylacetate (3 : 1) to yielding 5-OTBDMS-4"-*(R)*-4"-desoxy-4"-(2'''-Methyl-isoxazolidine-5'''-carboxylic acid methyl ester)-avermectin B_1.

Step B: 0.200 g of 5-OTBDMS-4"-*(R)*-4"-desoxy-4"-(2'''-methyl-isoxazolidine-5'''-carboxylic acid methyl ester)-avermectin B_1 are dissolved in 5 ml tetrahydrofuran, then 2 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a solution of sodium hydrogencarbonate and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane / ethylacetate,

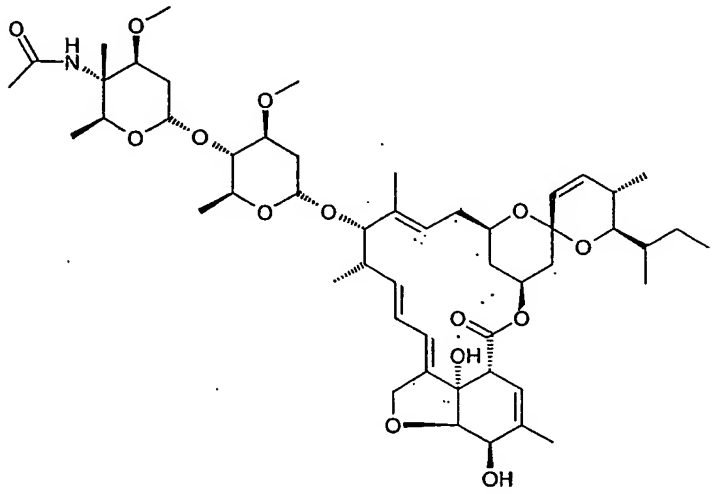
yielding 4"-*(R)*-4"-desoxy-4"-(2'"-methyl-isoxazolidine-5'"-carboxylic acid methyl ester)-avermectin B_1.

Example P7: 4"-*(R)*- 4"-desoxy -4"-N-methyl-N-(methylcarbonyloxy-amino)-4"-methyl-avermectin B1.



1080 mg 5-OTBDMS-4"-*(R)*- 4"-desoxy -4"-N-methyl-hydroxylamine-4"-methyl -avermectin B_1 (P3: Steps A and B) are dissolved in 20 ml dichloromethane, 1250 mg dimethylaminopyridine, 370 µl acetylchloride are added. The mixture is stirred at room temperature for 30 minutes. The reaction mixture is poured into saturated sodium hydrogencarbonate, extracted with ethylacetate, dried over Mg_2SO_4, and concentrated *in vacuo*. 300 mg of the residue is dissolved in 7.5 ml tetrahydrofuran, then 1.5 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into water, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4"-*(R)*- 4"-desoxy -4"-N-methyl-N-(methylcarbonyloxy-amino)-4"-methyl-avermectin B1.

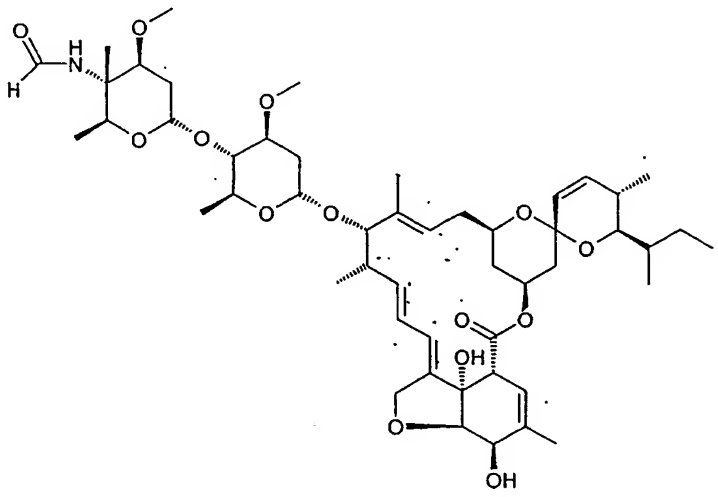
Example P8: 4"-*(S)*- 4"-desoxy -4"-acetylamino-4"-methyl-Avermectin B_1



Step A : To a solution of 0.2 g of 5-OTBDMS-4"-*(S)*- 4"-desoxy -4"-amino-4"-methyl-Avermectin B_1 (P1: Steps A to D) and 0.16 ml of pyridine in 4 ml tetrahydrofuran at room temperature is added 0.07 ml of acetyl chloride. The mixture is stirred for 1 hour. The mixture is poured into a saturated solution of sodium hydrogencarbonate and ethyl acetate, extracted with ethylacetate, dried over Na_2SO_4, and concentrated *in vacuo*. The 5-OTBDMS-4"-*(S)*- 4"-desoxy -4"-acetylamino-4"-methyl-Avermectin B_1 is used without further purification.

Step B: 5-OTBDMS-4"-*(S)*- 4"-desoxy -4"-acetylamino-4"-methyl-Avermectin B_1 is dissolved in 6 ml tetrahydrofuran, then 1 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into water, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ ethylacetate, yielding 4"-*(S)*- 4"-desoxy -4"-acetylamino-4"-methyl-Avermectin B_1.

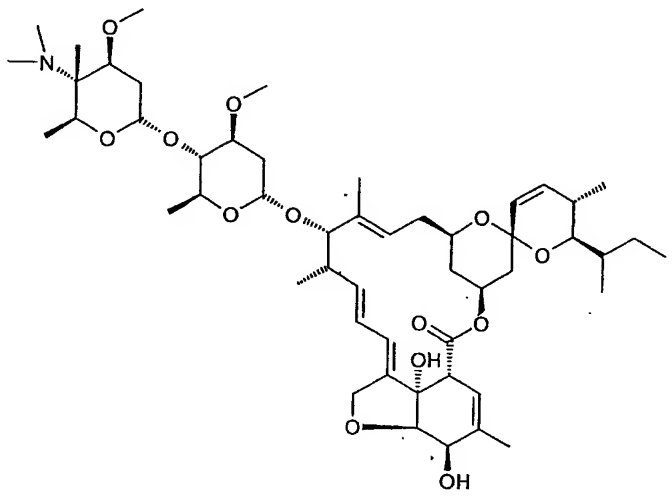
Example P9: 4"-*(S)*- 4"-desoxy -4"-formylamino-4"-methyl-Avermectin B_1



Step A : To a solution of 0.125 g of 5-OTBDMS-4"-*(S)*- 4"-desoxy -4"-amino-4"-methyl-Avermectin B_1 (P1: Steps A to D) in 6 ml ethylacetate and 12 ml of sodium hydrogencarbonate (1M) at room temperature is added 0.11 ml of acetic formic anhydride. The mixture is stirred for 1 hour. The mixture is poured into a saturated solution of sodium hydrogencarbonate and ethyl acetate, extracted with ethylacetate, dried over Na_2SO_4, and concentrated *in vacuo*. The 5-OTBDMS-4"-*(S)*- 4"-desoxy -4"-formylamino-4"-methyl-Avermectin is used without further purification.

Step B: 5-OTBDMS-4"-*(S)*- 4"-desoxy -4"-formylamino-4"-methyl-Avermectin is dissolved in 5 ml tetrahydrofuran, then 1 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into water, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with ethylacetate, yielding 4"-*(S)*- 4"-desoxy -4"-formylamino-4"-methyl-Avermectin B_1.

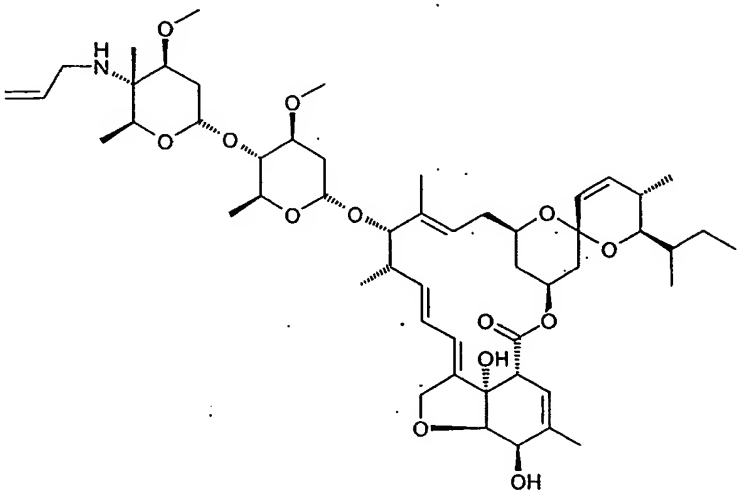
Example P10: 4"-*(S)*- 4"-desoxy -4"-N, N-dimethylamino-4"-methyl-Avermectin B_1



Step A : To a solution of 0.2 g of 5-OTBDMS-4"-*(S)*- 4"-desoxy -4" -amino-4"-methyl-Avermectin B_1 (P1: Steps A to D) and 0.162 mg of acid pivalic in acetonitrile at room temperature is added 0.08 ml of formaldehyde (37%). The mixture is stirred for 2 hours. Then 0.02 g of sodium cyanoborohydride is added. The mixture is stirred for 18 hours. The mixture is poured into a saturated solution of sodium hydrogencarbonate and ethylacetate, extracted with ethylacetate, dried over Na_2SO_4, and concentrated *in vacuo*. The 5-OTBDMS-4"-*(S)*- 4"-desoxy -4"-N, N-dimethylamino-4"-methyl-Avermectin B1 is used without further purification.

Step B: 5-OTBDMS-4"-*(S)*- 4"-desoxy -4"-N, N-dimethylamino-4"-methyl-Avermectin B1 is dissolved in 5 ml tetrahydrofuran, then 1 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into water, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with ethylacetate, yielding 4"-*(S)*- 4"-desoxy -4"-N, N-dimethylamino-4"-methyl-Avermectin B1.

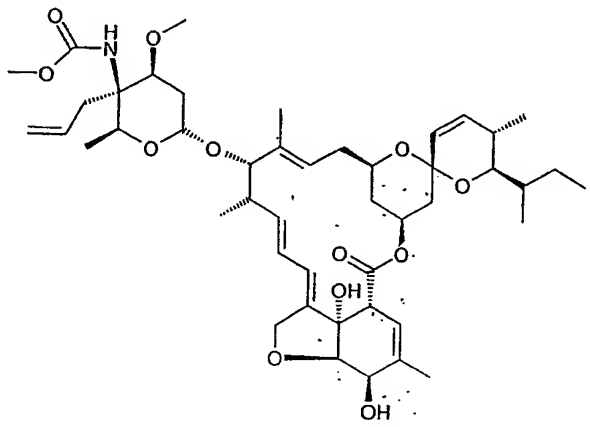
Example P11: 4"-*(S)*- 4"-desoxy -4"-N-allylamino-4"-methyl-Avermectin B_1



Step A : To a solution of 0.165 g of 5-OTBDMS-4"-*(S)*- 4"-desoxy -4" -amino-4"-methyl-Avermectin B_1 (P1: Steps A to D) and 0.138 mg of potassium carbonate in 8 ml acetonitrile is added 0.1 ml of allylbromide. The mixture is stirred for 3 hours at reflux. The mixture is poured into water and ethylacetate, extracted with ethylacetate, dried over Na_2SO_4, and concentrated *in vacuo*. The residue is used without further purification.

Step B: 5-OTBDMS-4"-*(S)*- 4"-desoxy -4"-N-allylamino-4"-methyl-Avermectin B1 (obtained from Step A) is dissolved in 5 ml tetrahydrofuran, then 1 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4"-*(S)*- 4"-desoxy -4"-N-allylamino-4"-methyl-Avermectin B_1.

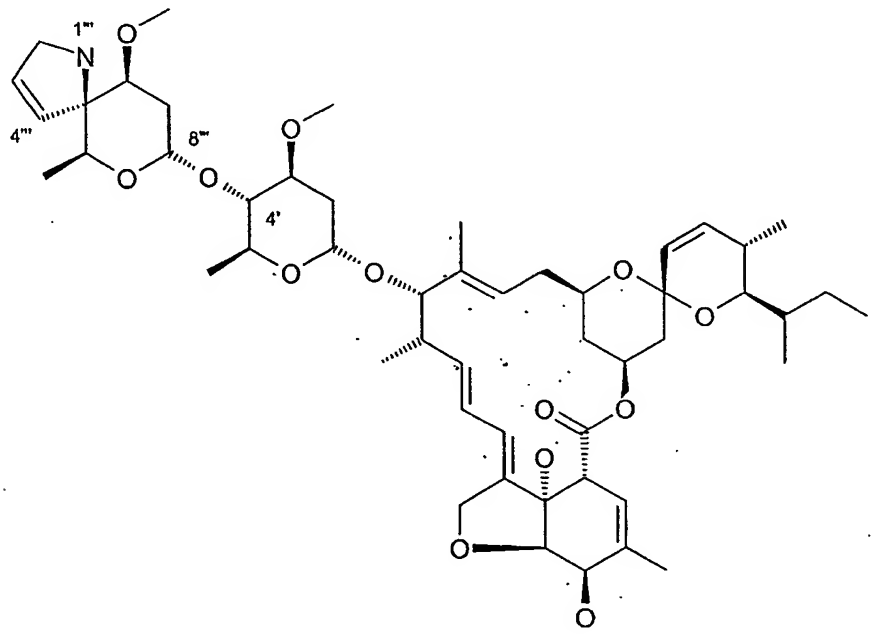
Example P12: 4'-*(R)*- 4'-desoxy -4'-methyloxycarbonylamino-4'-allyl-Avermectin B_1 monosaccharide.



Step A : To a solution of 0.3 g of 5-OTBDMS-4'-*(R)*- 4'-desoxy -4'-amino-4'-allyl-Avermectin B_1 monosaccharide (obtained by the same reactions that with the disaccharide derivative - P1: Steps A, B, C (Grignard is allylmagnesium bromide) and D) 6 ml of sodium hydrogencarbonate (1M) and 10 ml of ethylacetate at room temperature is added 0.06 ml of methyl chloroformate. The mixture is stirred for 1 hour. The mixture is poured into a saturated solution of sodium hydrogencarbonate and ethyl acetate, extracted with ethylacetate, dried over Na_2SO_4, and concentrated *in vacuo*. The residue is used without further purification.

Step B: 5-OTBDMS-4'-*(R)*- 4'-desoxy-4'-methyloxycarbonylamino-4'-allyl-Avermectin B_1 monosaccharide is dissolved in 8 ml tetrahydrofuran, then 1.6 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with ethylacetate, yielding 4'-*(R)*- 4'-desoxy-4'-methyloxycarbonylamino-4'-allyl-Avermectin B_1 monosaccharide.

Example P13: 4'-O-[(5'''R,6'''S,8'''S,10'''S)-10'''-Methoxy-6'''-methyl-7'''-oxa-1'''-aza-spiro[4.5]dec-3'''-en-8'''-yl]-avermectin B1 monosaccharide.

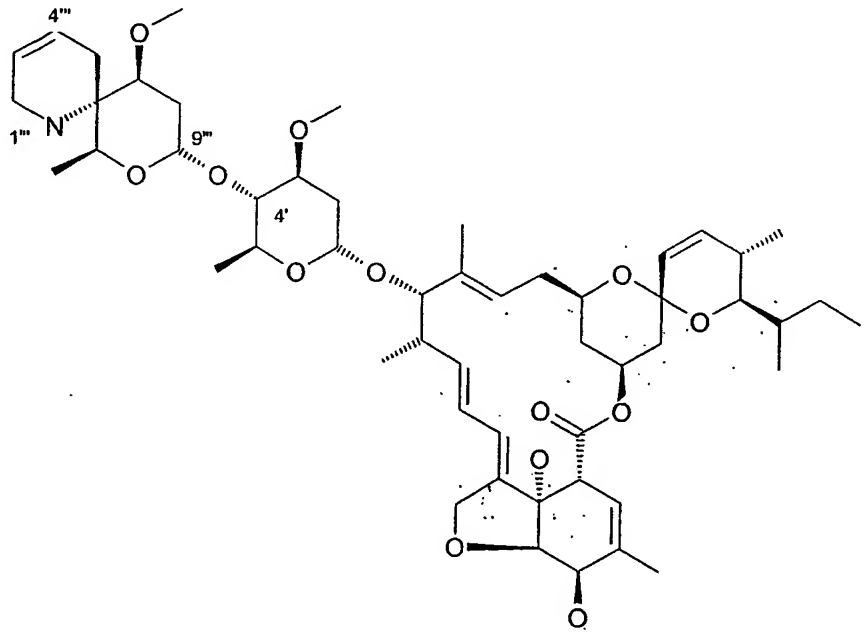


Step A : To a solution of 1 g of 5-OTBDMS-4"-*(R)*- 4"-desoxy- 4"-N-allylamino-4"-vinyl-Avermectin B_1 (P1: Steps A, B, C (Grignard is vinylmagnesium bromide) and D, and P11: Step A) in 50 ml of dichloromethane is added 0.07 ml of trifluoroacetic acid, 0.07 ml of tetraisopropyltitanium. The mixture is stirred for 1 hour at reflux. Then 0.1 g of Grubb's catalyst is added. The mixture is stirred for 24 hour at reflux, then 0.3 g of Grubb's catalyst and 0.14 ml of tetraisopropyltitanium are added. The mixture is stirred for 24 hour at reflux. The solvent is removed under vaccum and the residue is used without further purification.

Step B: 5-OTBDMS-4"-*(R)*- 4"-desoxy- 4"- (4",4'''-dihydro-1H-pyrrole) Avermectin B_1 (obtained from Step A) is dissolved in 25 ml tetrahydrofuran, then 10 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with

hexane/tetrahydrofuran, yielding 4"-*(R)*- 4"-desoxy- 4"- (4",4'"-dihydro-1H-pyrrole) Avermectin B_1.

Example P14: 4'-O-[(6'"S,7'"S,9'"S,11'"S)-11'"-Methoxy-7'"-methyl-8'"-oxa-1'"-aza-spiro[5.5]undec-3'"-en-9'"-yl]-avermectin B1 monosaccharide.

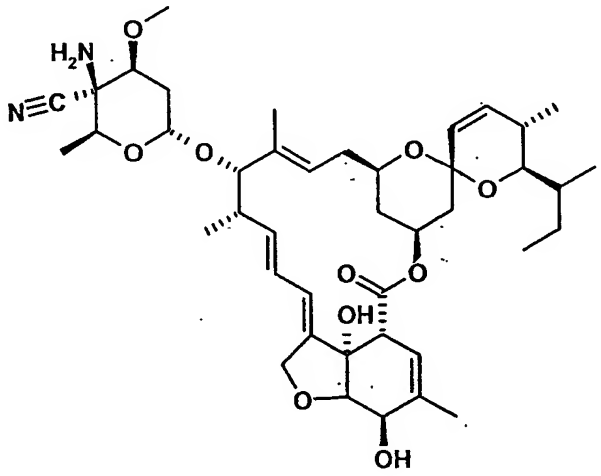


Step A : To a solution of 0.6 g of 5-OTBDMS-4"-*(S)*- 4"-desoxy- 4"-N-allylamino-4"-allyll-Avermectin B_1 (P1: Steps A, B, C (Grignard is allylmagnesium bromide) and D, and P11: Step A)in 30 ml of dichloromethane is added 0.05 ml of trifluoroacetic acid, 0.05 ml of tetraisopropyltitanium. The mixture is stirred for 1 hour at reflux. Then 0.06 g of Grubb's catalyst is added. The mixture is stirred for 24 hour at reflux, then 0.12 g of Grubb's catalyst and 0.10 ml of tetraisopropyltitanium are added. The mixture is stirred for 24 hour at reflux. The solvent is removed under vaccum and the residue is used without further purification.

Step B: 5-OTBDMS-4"-*(S)*- 4"-desoxy- 4"- (1'", 4", 3'", 6'"-tetrahydro-pyridine) Avermectin B_1 (obtained from Step A) is dissolved in 15 ml tetrahydrofuran, then 6 ml of a stock solution are added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with

ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/tetrahydrofuran (1/2), yielding 4"-*(S)*- 4"-desoxy- 4"- (1"', 4", 3"', 6"'-tetrahydro-pyridine) Avermectin B_1.

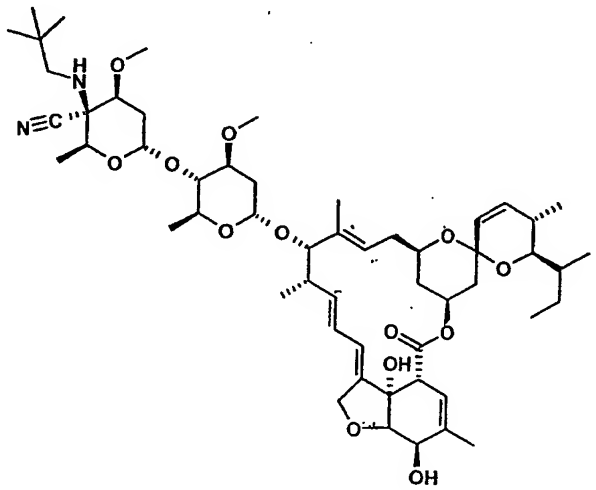
Example P15: 4'-(R)-4'-desoxy-4'-amino-4'-cyano-avermectin B1 monosaccharide



Step A: 3.0 g 4'-oxo-5-O-*t*-butyldimethylsilyl-avermectin B1 monosaccharide are dissolved in 20 ml ethyl acetate, then 2.14 ml hexamethyldisilazane and 450 mg zinc chloride are added. The mixture is stirred at 50 °C for 4 hours. Then 600 mg trimethylsilyl cyanide are added. Stirring is continued at 50 °C for additional 3 hours. Then the reaction mixture is cooled to room temperature, extracted with water and ethyl acetate, the organic phase dried with sodium sulfate and the solvent evaporated.

Step B: The crude product from Step A is dissolved in 20 ml methanol, the solution cooled to 0 °C, and 0.21 ml methanesulfonic acid are added. The mixture is stirred at 0 °C for 30 minutes, then 20 ml aqueous 1N sodium bicarbonate are added, and the mixture extracted with ethyl acetate. The organic phase is dried with sodium sulfate and the solvent evaporated. The residue is purified by chromatography on silica gel with hexane/ethyl acetate, yielding 4'-(R)-4'-desoxy-4'-amino-4'-cyano-avermectin B1 monosaccharide.

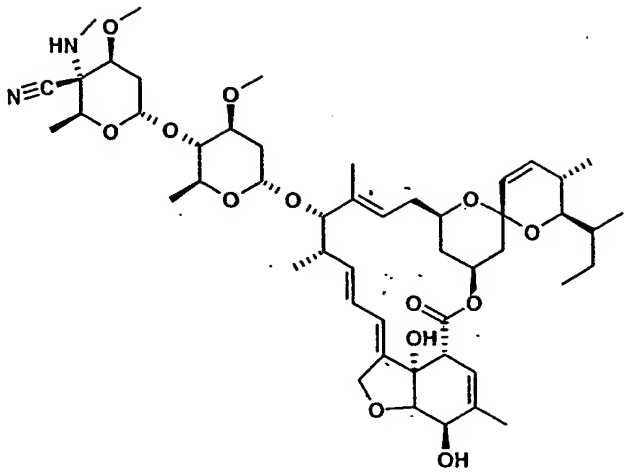
Example P16: 4"-(R)-4"-desoxy-4"-(2,2-dimethyl-propylamino)-4"-cyano-avermectin B1



Step A: 4.0 g 4"-oxo-5-O-*t*-butyldimethylsilyl-avermectin B1 are dissolved in 30 ml toluene, then 2.1 g 2,2-dimethyl-propylamine, 1.0 g zinc chloride and 0.93 ml trimethylsilyl chloride are added. The mixture is stirred at 50 °C for 4 hours. Then 1.9 ml trimethylsilyl cyanide are added. Stirring is continued at 50 °C for additional 3 hours. Then the reaction mixture is cooled to room temperature, extracted with water and ethyl acetate, the organic phase dried with sodium sulfate and the solvent evaporated.

Step B: The crude product from Step A is dissolved in 40 ml methanol, the solution cooled to 0 °C, and 0.36 ml methanesulfonic acid are added. The mixture is stirred at 0 °C for 30 minutes, then 40 ml aqueous 1N sodium bicarbonate are added, and the mixture extracted with ethyl acetate. The organic phase is dried with sodium sulfate and the solvent evaporated. The residue is purified by chromatography on silica gel with hexane/ethyl acetate, yielding 4"-(R)-4"-desoxy-4"-(2,2-dimethyl-propylamino)-4"-cyano-avermectin B1.

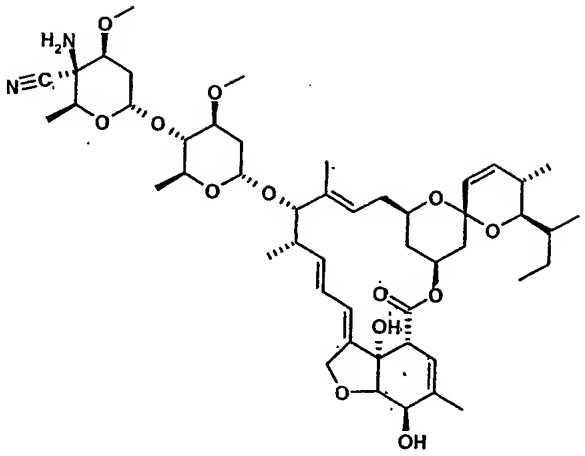
Example P17: 4"-(S)-4"-desoxy-4"-methylamino-4"-cyano-avermectin B1



Step A: 2.0 g 4"-oxo-5-O-*t*-butyldimethylsilyl-avermectin B1 are dissolved in 10 ml ethyl acetate, then 1.5 ml heptamethyldisilazane and 300 mg zinc chloride are added. The mixture is stirred at 50 °C for 4 hours. Then 600 mg trimethylsilyl cyanide are added. Stirring is continued at 50 °C for additional 3 hours. Then the reaction mixture is cooled to room temperature, extracted with water and ethyl acetate, the organic phase dried with sodium sulfate and the solvent evaporated.

Step B: The crude product from Step A is dissolved in 10 ml methanol, the solution cooled to 0 °C, and 0.08 ml methanesulfonic acid are added. The mixture is stirred at 0 °C for 45 minutes, then 10 ml aqueous 1N sodium bicarbonate are added, and the mixture extracted with ethyl acetate. The organic phase is dried with sodium sulfate and the solvent evaporated. The residue is purified by chromatography on silica gel with hexane/ethyl acetate, yielding 4"-(S)-4"-desoxy-4"-methylamino-4"-cyano-avermectin B1.

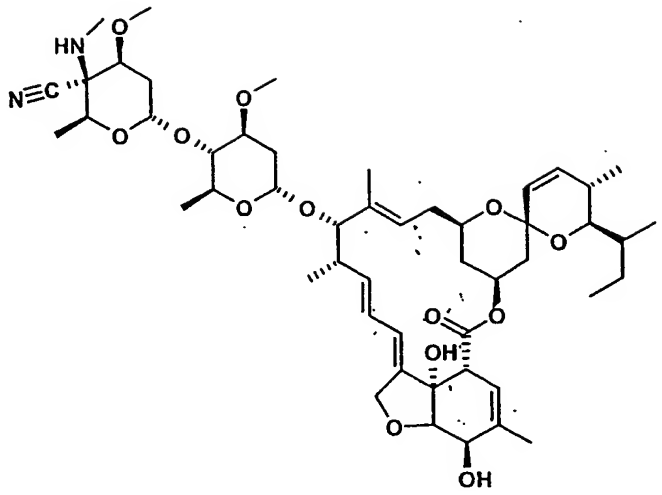
Example P18: 4"-(R)-4"-desoxy-4"-amino-4"-cyano-avermectin B1



Step A: 2.0 g 4"-oxo-5-O-*t*-butyldimethylsilyl-avermectin B1 are dissolved in 10 ml ethyl acetate, then 1.4 ml hexamethyldisilazane and 300 mg zinc chloride are added. The mixture is stirred at 50 °C for 4 hours. Then 400 mg trimethylsilyl cyanide are added. Stirring is continued at 50 °C for additional 3 hours. Then the reaction mixture is cooled to room temperature, extracted with water and ethyl acetate, the organic phase dried with sodium sulfate and the solvent evaporated.

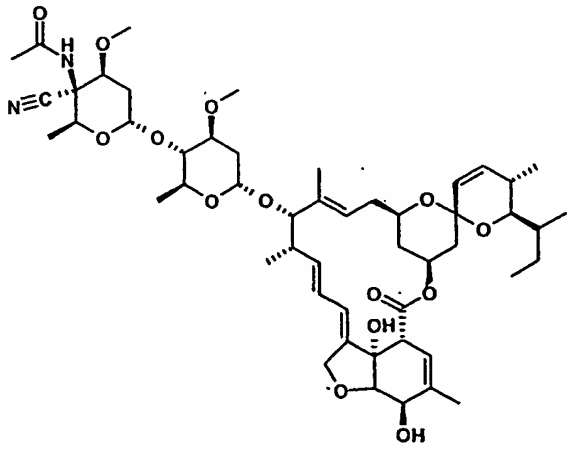
Step B: The crude product from Step A is dissolved in 20 ml methanol, the solution cooled to 0 °C, and 0.12 ml methanesulfonic acid are added. The mixture is stirred at 0 °C for 45 minutes, then 20 ml aqueous 1N sodium bicarbonate are added, and the mixture extracted with ethyl acetate. The organic phase is dried with sodium sulfate and the solvent evaporated. The residue is purified by chromatography on silica gel with hexane/ethyl acetate, yielding 4"-(R)-4"-desoxy-4"-amino-4"-cyano-avermectin B1.

Example P19: 4"-(R)-4"-desoxy-4"-methylamino-4"-cyano-avermectin B1



2.0 g 4"-(R)-4"-desoxy-4"-amino-4"-cyano-avermectin B1 (P18) are dissolved in 20 ml ethyl acetate, then 16 ml methyliodide and 20 ml aqueous 1N sodium bicarbonate are added. The mixture is stirred vigorously at 60 °C for 18 hours. Then the reaction mixture is cooled to room temperature, the phases separated, the organic phase dried with sodium sulfate and the solvent evaporated. The residue is purified by chromatography on silica gel with hexane/ethyl acetate, yielding 4"-(R)-4"-desoxy-4"-methylamino-4"-cyano-avermectin B1.

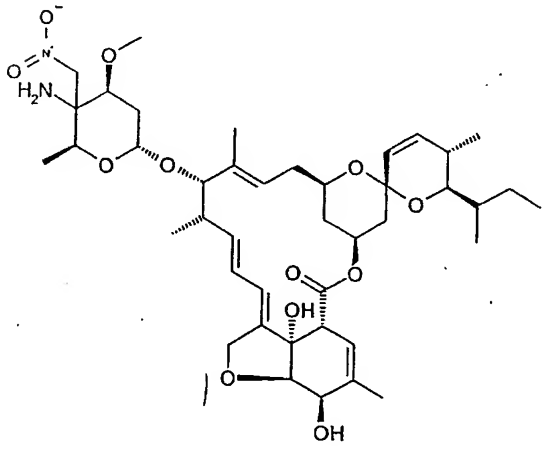
Example P20: 4"-(R)-4"-desoxy-4"-acetylamino-4"-cyano-avermectin B1



3.0 g 4"-(R)-4"-desoxy-4"-amino-4"-cyano-avermectin B1 (P18) are dissolved in 20 ml ethyl acetate, then 20 ml aqueous 1N sodium bicarbonate are added. The mixture is stirred

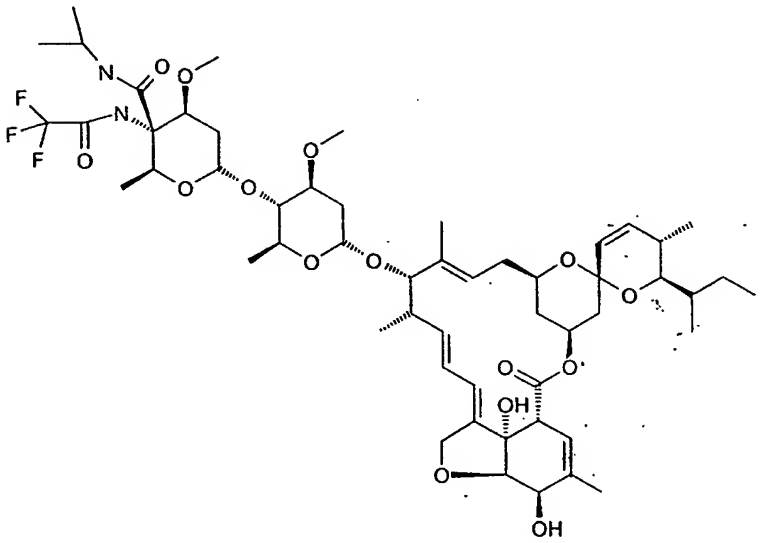
vigorously and 1.6 ml acetylchloride are added. Stirring is continued at room temperature for 4 hours. Then the phases are separated, the organic phase is dried with sodium sulfate and the solvent evaporated. The residue is purified by chromatography on silica gel with hexane/ethyl acetate, yielding 4"-(R)-4"-desoxy-4"-acetylamino-4"-cyano-avermectin B1.

Example P21: 4'-(R)-4'-desoxy-4'-amino-4'-nitromethyl-avermectin B1 monosaccharide and 4'-(S)-4'-desoxy-4'-amino-4'-methylnitro-avermectin B1 monosaccharide.



Step A: To a solution of 13g of 5-OTBDMS-4'-desoxy-4'-phenylsulfinimine-Avermectin B_1 (obtained by the method described in step A and B : Exemple P1) in 110 ml of nitromethane at RT is added 5900 µl of piperidine. The mixture is stirred at room temperature for 1 hour. Then, the solvents are distilled off. The residue is dissolved in methanol at 0°C then 5 eq. of methanesulfonic acid were added. The mixture is stirred at 0 °C for 30 minutes, then saturated solution of sodium bicarbonate is added, and the mixture extracted with ethyl acetate. The organic phase is dried with sodium sulfate and the solvent evaporated. The residue is purified by chromatography on silica gel with cyclohexane/ethyl acetate, yielding 4'-(R)-4'-desoxy-4'-amino-4'-methylnitro-avermectin B1 monosaccharide and 4'-(S)-4'-desoxy-4'-amino-4'-methylnitro-avermectin B1 monosaccharide.

Example P22: 4"-(S)-4"-desoxy-4"-trifluoroacetylamino-4"- isopropylcarbamoyl-avermectin B1

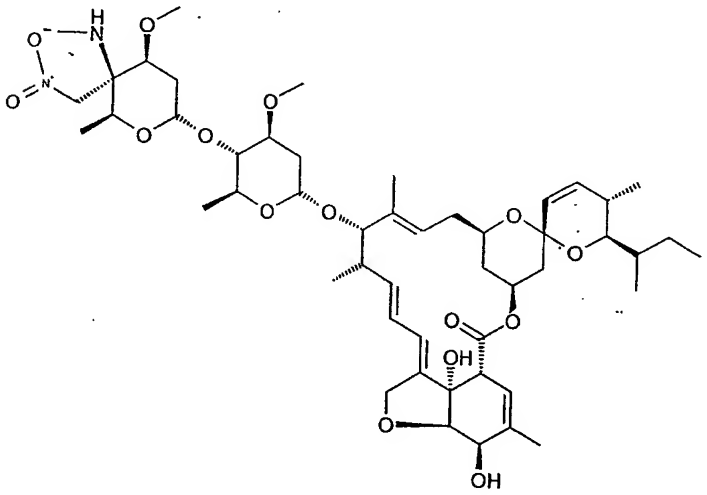


Step A: To a solution of 7.39g of 5-OTBDMS-4"-desoxy-4"-phenylsulfinimine-Avermectin B_1 (obtained in step A, B : Exemple P1) in 150 ml of dichloromethane at -78°C is added 1970 µl of Pyridine, 840 µl of isopropylisocyanide and 940 µl of trifluoroacetic acid. The mixture is stirred overnight at room temperature. The mixture is poured into a saturated sodium hydrogenocarbonate and ethylacetate, extracted with ethylacetate; the organic phase is dried over sodium sulfate, and concentrated *in vacuo*. The residue is purified by chromatography on silica gel with cyclohexane/ethyl acetate, yielding 5-O-*t*-butyldimethylsilyl-4"-(S)-4"-desoxy-4"-trifluoroacetylamino-4"- isopropylcarbamoyl-avermectin B1.

Step B: 5-O-*t*-butyldimethylsilyl-4"-(S)-4"-desoxy-4"-trifluoroacetylamino-4"- isopropylcarbamoyl-avermectin B1. (obtained from Step A) is dissolved in 5 ml tetrahydrofuran, then 1 ml of a stock solution is added, which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography

on silica gel with hexane/ethylacetate, yielding : 4"-(S)-4"-desoxy-4"-trifluoroacetylamino-4"-isopropylcarbamoyl-avermectin B1.

Example P23: 4"-(R)-4"-desoxy-4"-amino-N-methyl-4"- nitromethyl -avermectin B1.

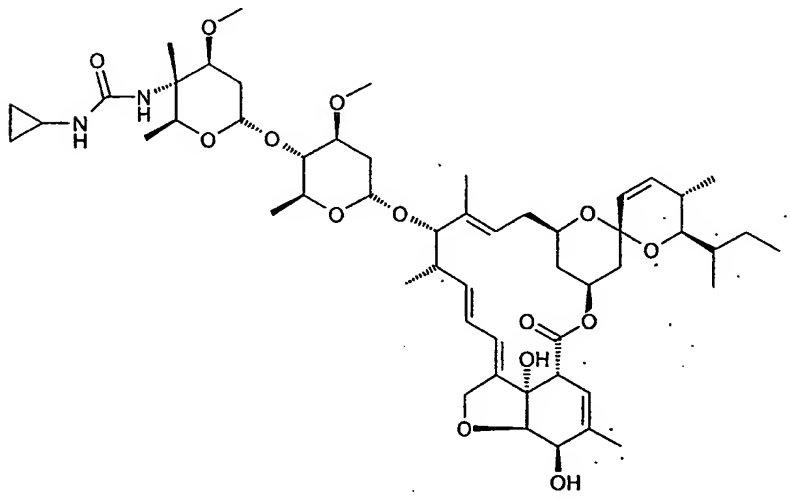


Step A: 3 g 4"-oxo-5-O-*t*-butyldimethylsilyl-avermectin B1 are dissolved in 20 ml ethyl acetate, then 1.82g heptamethyldisilazane and 430 mg zinc chloride are added. The mixture is stirred at 70 °C for 3 hours. Then the solvents are distilled off. The crude residue is dissolved in 10 ml of nitromethane and 440 µl of piperidine is added. The mixture is stirred at room temperature overnight. The solvents are distilled off and the residue is purified by chromatography on silica gel with cyclohexane/ethylacetate, yielding 5-O-*t*-butyldimethylsilyl-7-trimethylsilyl-4"-(R)-4"-desoxy-4"-amino-N-methyl-4"-methylnitro-avermectin B1.

Step B: 5-O-*t*-butyldimethylsilyl-7-trimethylsilyl-4"-(R)-4"-desoxy-4"-amino-N-methyl-4"-methylnitro-avermectin B1. (obtained from Step A) is dissolved in tetrahydrofuran (2.5 mL by 01g), then a stock solution is added (0.5 mL by 01g of starting material), which is

prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with cyclohexane/ethylacetate, yielding 4"-(R)-4"-desoxy-4"-amino-N-methyl-4"-methylnitro-avermectin B1.

Example P24: 4"-*(S)* -4"-desoxy-4"-(cyclopropylaminocarbonyl-amino)-4"-methyl-Avermectin B_1



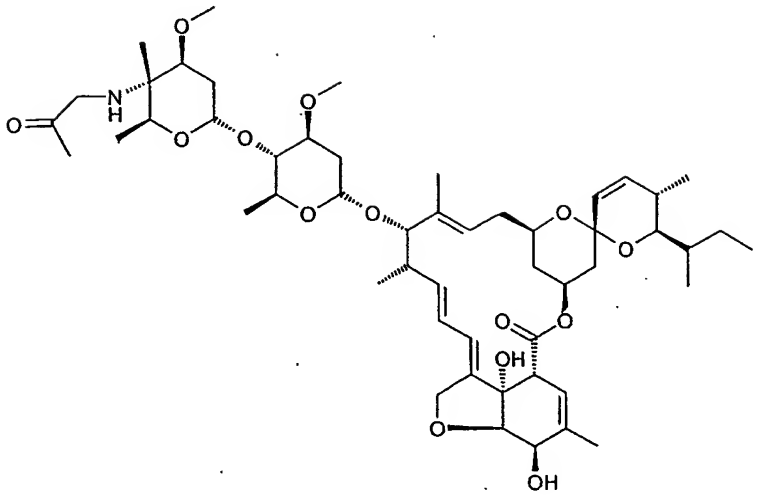
Step A : To a solution of 1 g of 5-OTBDMS-4"-*(S)*- 4"-desoxy -4"-amino-4"-methyl-Avermectin B_1 (P1: Steps A to D) and 1.4 ml of triethylamine in 20 ml dichloromethane at room temperature is added 1g of p-nitrophenyl chloroformate. The mixture is stirred for 45 minutes. The mixture is poured into a saturated solution of sodium hydrogencarbonate and dichloromethane, washed with water (2x), dried over Na_2SO_4, and concentrated *in vacuo*. The 5-OTBDMS-4"-*(S)*- 4"-desoxy -4"- carbamic acid p-nitrophenyl ester-4"-methyl-Avermectin B_1 is used without further purification.

Step B: 5-OTBDMS-4"-*(S)*- 4"-desoxy -4"- carbamic acid p-nitrophenyl ester-4"-methyl-Avermectin B_1. (obtained from Step A) is dissolved in tetrahydrofuran (2.5 mL by 0.1g), then a stock solution is added (0.5 mL by 0.1g of starting material), which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4"-*(S)*- 4"-desoxy -4"- carbamic acid p-nitrophenyl ester-4"-methyl-Avermectin B_1.

Step C : To a solution of 1 g of 4"-*(S)*- 4"-desoxy -4"- carbamic acid p-nitrophenyl ester-4"-methyl-Avermectin B_1. (Step B) and 0.18 ml of triethylamine in 10 ml dichloromethane at room temperature is added 45 µl of cyclopropylamine. The mixture is stirred for 30 minutes. The mixture is concentrated *in vacuo* and the residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4"-*(S)* -4"-desoxy-4"-cyclopropyl-urea-4"-methyl-Avermectin B_1.

Using the same reaction, it is possible to reverse the order of step B and C.

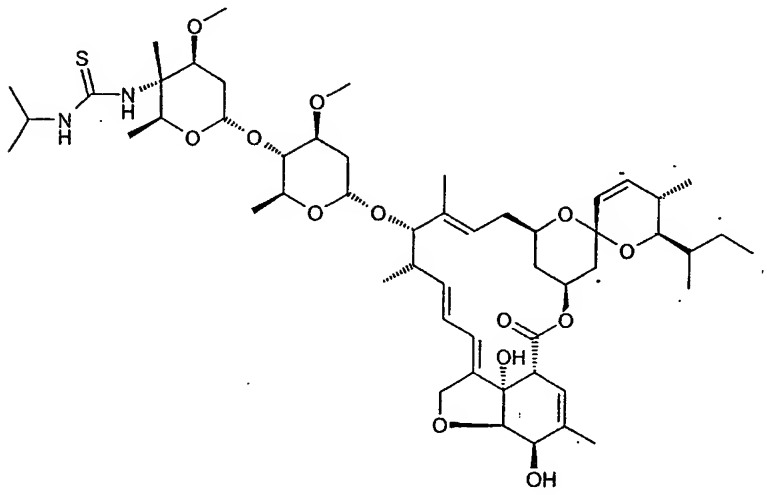
Example P25: 4"-*(S)* -4"-desoxy-4"- (propan-2-on-1-yl-amino)-4"-methyl-Avermectin B_1



Step A : To a solution of 0.420 mg g of 5-OTBDMS-4"-*(S)* -4"-desoxy-4"- amino -4"-methyl-Avermectin B_1 in 5 ml of ethylacetate at room temperature and 5 ml of sodium hydrogencarbonate (1M) is added 380 µl of methylbromoacetate. The mixture is stirred overnight. The aqueous phase and the organic phase are separated. The organic phase mixture is washed with water and concentrated *in vacuo*. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 5-OTBDMS-4"-*(S)* -4"-desoxy-4"- amino propan-2-one-4"-methyl-Avermectin B_1.

Step B: 5-OTBDMS-4"-*(S)* -4"-desoxy-4"- amino propan-2-one-4"-methyl-Avermectin B_1 (obtained from Step A) is dissolved in tetrahydrofuran (2.5 mL by 0.1g), then a stock solution is added (0.5 mL by 0.1g of starting material), which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4"-*(S)* -4"-desoxy-4"- amino propan-2-one-4"-methyl-Avermectin B_1.

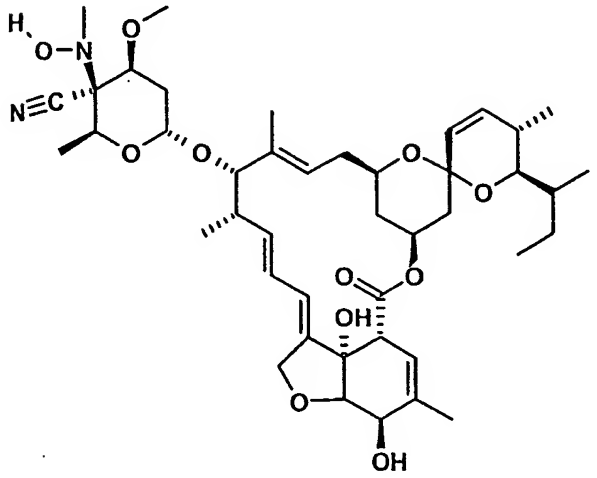
Example P26: 4"-*(S)* -4"-desoxy-4"-(isopropylaminothiocarbonyl-amino)-4"-methyl-Avermectin B_1



Step A : To a solution of 0.2 g of 5-OTBDMS-4"-*(S)* -4"-desoxy-4"- amino -4"-methyl-Avermectin B_1 in 3 ml tetrahydrofuranne at room temperature is added 220 mg of isopropyl isothiocyanate. The mixture is stirred overnight at room temperature. The mixture is concentrated *in vacuo* and the residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 5-OTBDMS-4"-*(S)* -4"-desoxy-4"-isopropyl-thiourea-4"-methyl-Avermectin B_1.

Step B: 5-OTBDMS-4"-*(S)* -4"-desoxy-4"-isopropyl-thiourea-4"-methyl-Avermectin B_1 (obtained from Step A) is dissolved in tetrahydrofuran (2.5 mL by 0.1g), then a stock solution is added (0.5 mL by 0.1g of starting material), which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4"-*(S)* -4"-desoxy-4"-isopropyl-thiourea-4"-methyl-Avermectin B_1.

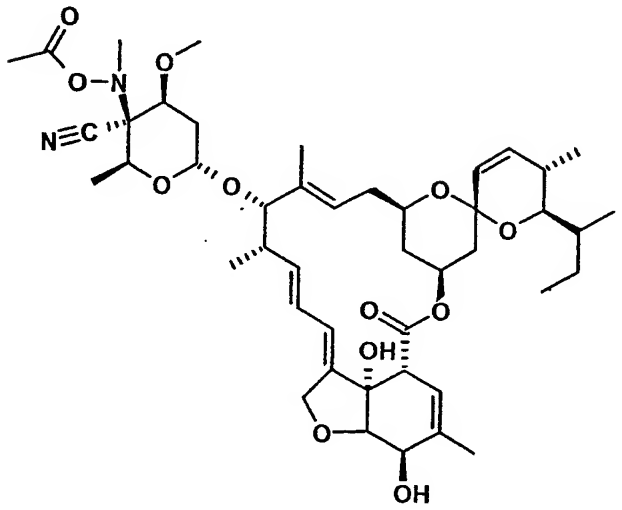
Example P27 : 4'-(R)-4'-desoxy-4'- N-methyl-N-hydroxy-amino-4'-cyano-avermectin B1 monosaccharide



Step A: To a solution of 3020 mg of 5-OTBDMS-4"-desoxy-4"-methyloxidoimino - Avermectin B_1 (obtained from avermectin B1 monosaccharide by analogy with Example P3, step A) in 80 ml of dichloromethane at RT is added 2190 µl of trimethylsilylcyanide. The mixture is stirred at room temperature for 4 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is washed with water and dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 5-OTBDMS-4'-(R)-4'-desoxy-4'- N-methyl-N-oxy-amino-4'-cyano-avermectin B1 monosaccharide.

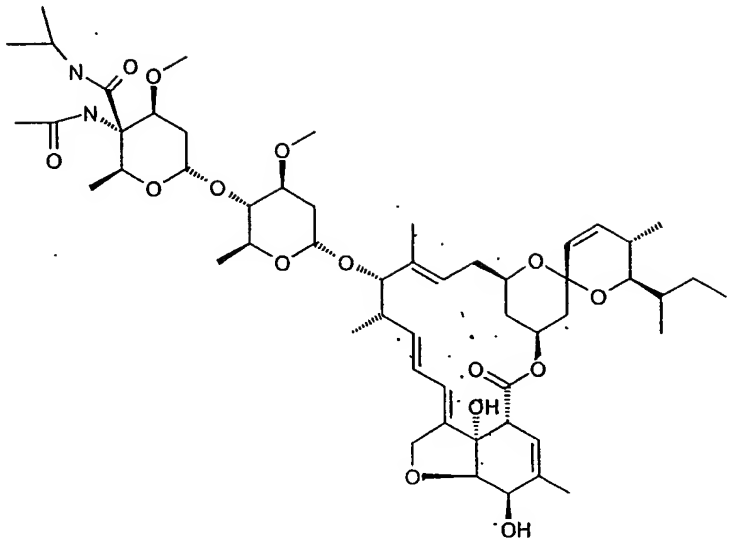
Step B: 5-OTBDMS-4'-(R)-4'-desoxy-4'- N-methyl-N-oxy-amino-4'-cyano-avermectin B1 monosaccharide (obtained from Step A) is dissolved in tetrahydrofuran (2.5 mL by 0.1g), then a stock solution is added (0.5 mL by 0.1g of starting material), which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4'-(R)-4'-desoxy-4'- N-methyl-N-oxy-amino-4'-cyano-avermectin B1 monosaccharide.

Example P28 : 4'-(R)-4'-desoxy-4'- N-methyl-N-(methylcarbonyloxy-amino)-4'-cyano-avermectin B1 monosaccharide.



300 mg 5-OTBDMS-4'-(R)-4'-desoxy-4'- N-methyl-N-oxy-amino-4'-cyano-avermectin B1 monosaccharide (P27: Steps A) are dissolved in 6 ml dichloromethane, and 410 mg dimethylaminopyridine and 125 µl acetylchloride are added. The mixture is stirred at room temperature for 1 hour. The reaction mixture is filtered into silica gel with ethyl acetate and concentrated under vacuum. The residue is dissolved in tetrahydrofuran (2.5 mL by 0.1g), then a stock solution is added (0.5 mL by 0.1g of starting material), which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4'-(R)-4'-desoxy-4'- N-methyl-N-(methylcarbonyloxy-amino)-4'-cyano-avermectin B1 monosaccharide.

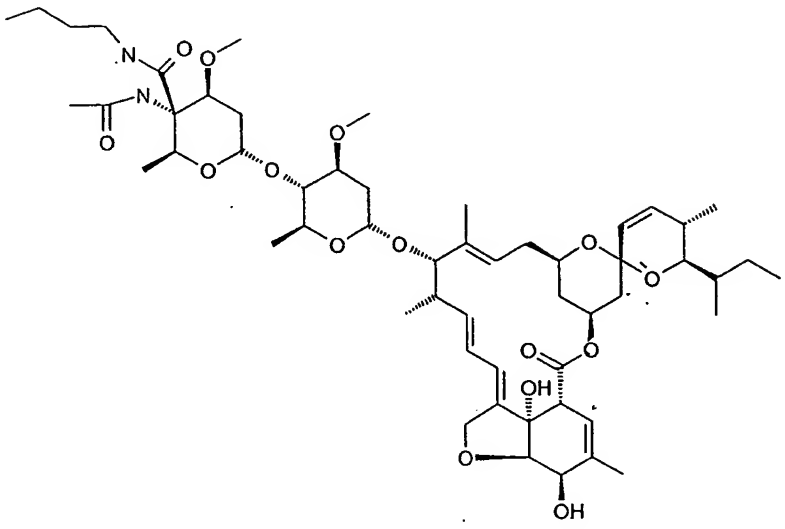
Example P29: 4"-(S)-4"-desoxy-4"-acetylamino-4"- isopropylcarbamoyl-avermectin B1.



Step A: 2 g 5-OTBDMS-4"-desoxy-4"-oxo-avermectin B1 are dissolved in 4 ml methanol and the mixture is stirred at room temperature for 30 minutes. Then 0.15 g of ammoniumacetate and 0.19 ml of isopropylisocyanide are added. The mixture is stirred at room temperature for 20 hours. The mixture is poured into ethyl acetate and washed two times with a saturated solution of sodium hydrogencarbonate. Then the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding a mixture of 5-OTBDMS-4"-(S)-4"-desoxy-4"-acetylamino-4"- isopropylcarbamoyl-avermectin B1. and 5-OTBDMS-4"-(S)-4"-O-acetyl-4"- isopropylcarbamoyl-avermectin B1.

Step B: 1.1 g of the mixture (obtained from Step A) is dissolved in 35 ml of tetrahydrofuran, then 2.1 mL of a stock solution are added (which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine) and 6.1 mL of pyridine. The mixture is stirred at room temperature for 20 hours, poured into an aqueous solution of 5% of sodium hydrogencarbonate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with hexane/ethylacetate, yielding 4"-(S)-4"-desoxy-4"-acetylamino-4"- isopropylcarbamoyl-avermectin B1.

Example P30: 4"-(S)-4"-desoxy-4"-acetylamino-4"- butylcarbamoyl-avermectin B1.



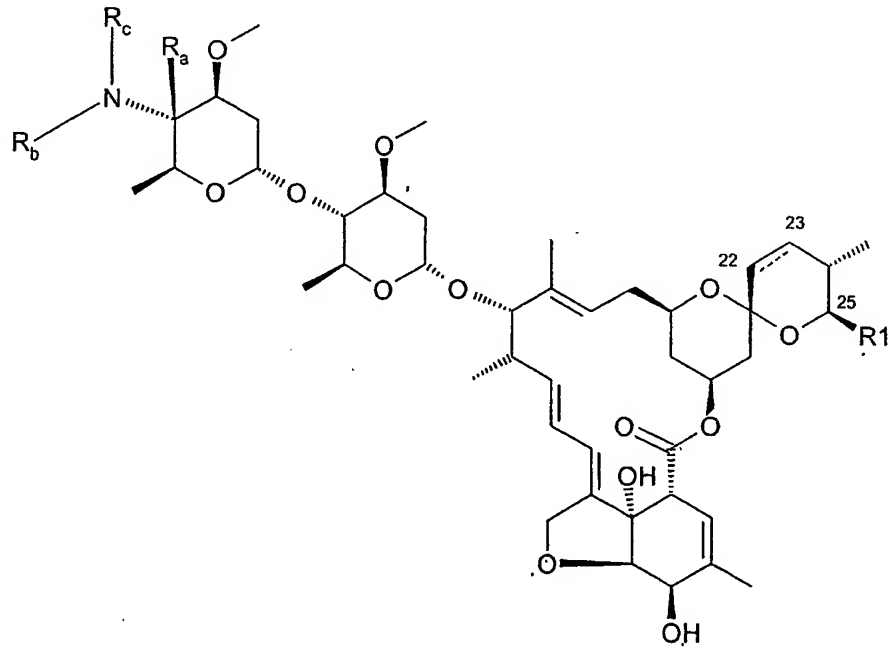
Step A: 2.03 g 5-OTBDMS-4"-(S)-4"-desoxy-4"-trifluoroacetylamino-4"- butylcarbamoyl-avermectin B1 are dissolved in 50 ml ethanol and 500 mg of sodium borohydride are added. The mixture is stirred at room temperature for 3 hours. Then 6 ml of a solution of sodium hydrogenocarbonate is added. The mixture is filtered and the solvents are distilled off. The residue is purified by chromatography on silica gel with ethylacetate/methanol, yielding 5-OTBDMS-4"-(S)-4"-desoxy-4"-amino-4"- butylcarbamoyl-avermectin B1 (not pur, 80% of purity).

Step B: 0.2 g 5-OTBDMS-4"-(S)-4"-desoxy-4"-amino-4"- butylcarbamoyl-avermectin B1 are dissolved in 5.0 ml tetrahydrofuran. 120 µl of pyridine and 50 µl of acetylchloride are added. The mixture is stirred at room temperature for 30 minutes. The mixture is poured into ethyl acetate and washed two times with a saturated solution of sodium hydrogencarbonate. Then the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with cyclohexane/ethylacetate, yielding 5-OTBDMS -4"-(S)-4"-desoxy-4"-acetylamino-4"- butylcarbamoyl-avermectin B1.

Step C: 5-OTBDMS -4"-(S)-4"-desoxy-4"-acetylamino-4"- butylcarbamoyl-avermectin B1 (obtained from Step B) is dissolved in tetrahydrofuran (2.5 mL by 0.1g), then a stock solution is added (0.5 mL by 0.1g of starting material), which is prepared from 250 g 70% HF-Pyridine, 275 ml tetrahydrofuran and 125 ml pyridine. The mixture is stirred at room temperature for 24 hours, poured into a mixture of saturated sodium hydrogencarbonate and ethylacetate, and extracted with ethylacetate. Then the phases are separated; the organic phase is dried over sodium sulfate and the solvents are distilled off. The residue is purified by chromatography on silica gel with cyclohexane/ethylacetate, yielding 4"-(S)-4"-desoxy-4"-acetylamino-4"- butylcarbamoyl-avermectin B1.

The compounds of Tables 1-96, A-L and M1-M8 can be prepared in the same way as described in Examples P1 to P30, or by methods known to a person skilled in the art.

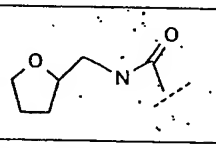
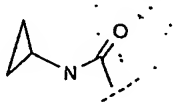
Table A: A compound of the formula

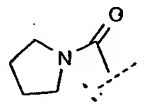


wherein R_1 is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

	LC-MS	R_a	R_b	R_c	Retention time (min)

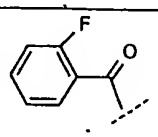
					B1a	B1b
Table A1	W	CH_3	H	H	5.71	5.39
Table A2	W	vinyl	H	H	6.03	5.55
Table A3	W	Allyl	H	H	6.13	5.87
Table A4	W	$PhCH_2$	H	H	6.24	-
Table A5	Z	CH_3	$CH_3C(O)$	H	10.08	9.23
Table A6	W	vinyl	$CH_3C(O)$	H	10.69	9.82
Table A7	W	Allyl	$CH_3C(O)$	H	11.80	11.00
Table A8	W	CH_3	HC(O)	H	10.08	-
Table A9	W	vinyl	HC(O)	H	10.67	9.76
Table A10	W	Allyl	HC(O)	H	11.65	-
Table A11	W	CH_3	$CH_3OC(O)$	H	11.22	10.44
Table A12	W	CH_3	$CH_3CH_2OC(O)$	H	11.31	10.67
Table A13	W	CH_3	$CH_3OCH_2C(O)$	H	11.04	-
Table A14	W	CH_3	$(CH_3)_2NCH_2C(O)$	H	5.97	5.60
Table A15	W	CH_3	$ClCH_2C(O)$	H	10.41	9.60
Table A16	W	CH_3	$CH_3C(O)OCH_2C(O)$	H	9.70	8.91
Table A17	W	CH_3	$CH_3SCH_2C(O)$	H	10.54	9.87
Table A18	W	CH_3	$NCCH_2C(O)$	H	9.39	8.70
Table A19	Z	CH_3	2-$PySCH_2C(O)$	CH_3	12.94	12.51
Table A20	Z	CH_3	$CH_3OCH_2CH_2C(O)$	H	11.45	10.69
Table A21	Z	CH_3	$CH_3CH_2OCH_2C(O)$	H	12.57	12.02
Table A22	W	CH_3	CH_3	CH_3	5.92	5.60
Table A23	W	$PhCH_2$	CH_3	CH_3	7.25	6.88
Table A24	X	CH_3	H_2NSO_2	H	10.85	-
Table A25	W	vinyl	allyl	H	10.40	10.14
Table A26	W	allyl	allyl	H	7.20	6.72
Table A27	W	Allyl	Propargyl	H	6.85	6.58
Table A28	W	CH_3	allyl	H	4.17	3.91

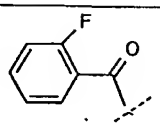
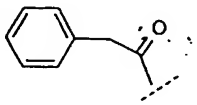
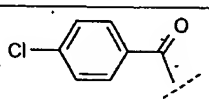
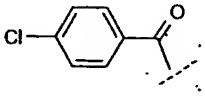
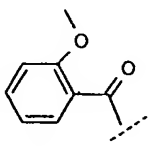
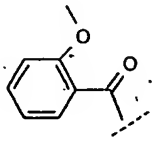
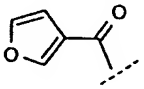
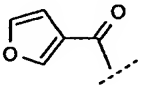
	LC - MS	R_a	R_b	R_c	Retention time (min)	
					B1a	B1b
Table A29	Z	CH_3	CH_3	H	4.99	-
Table A30	W	CN	iPrC(O)	CH_3	10.53	-
Table A31	W	CN	$CH_3OC(O)$	CH_3	11.84	11.20
Table A32	W	CN	EtC(O)	CH_3	9.87	9.20
Table A33	W	CN	EtOC(O)	CH_3	11.18	10.54
Table A34	W	CN	$(CH_2CH_2)CHC(O)$	CH_3	10.24	9.59
Table A35	W	CN	$CH_3CHCHC(O)$	CH_3	11.90	-
Table A36	W	CN	HC(O)	CH_3	9.14	8.48
Table A37	W	CN	$CH_3C(O)$	CH_3	9.50	8.85
Table A38	W	CN	$CH_3OCH_2C(O)$	CH_3	9.31	8.59
Table A39	W	CN	$(CH_3)_2CCHC(O)$	CH_3	10.48	9.84
Table A40	W	CN	CH_3	CH_3	12.04	11.42
Table A41	Z	CH_3	$CH_3CH_2CH_2CO$	H	12.78	12.25
Table A42	Z	CH_3	$C(O)SCH_2CH_2OCH_3$	H	13.35	12.98
Table A43	Z	CH_3	$C(O)SCH(CH_3)_2$	H	13.72	13.40
Table A44	Z	CH_3	C(O)SEt	H	13.45	13.13
Table A45	Z	CH_3		H	12.06	11.26
Table A46	Z	CH_3	EtONHC(O)	H	12.43	11.79
Table A47	Z	CH_3	$CH_3ONHC(O)$	H	11.75	11.0
Table A48	Z	CH_3	$CH_3OCH_2CH_2NHC(O)$	H	11.48	10.73
Table A49	Z	CH_3		H	12.23	11.48
Table A50	Z	CH_3	$CH_3CH_2CH_2NHC(O)$	H	12.80	12.26

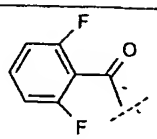
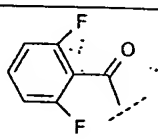
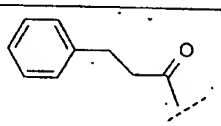
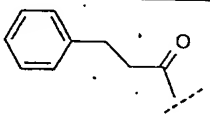
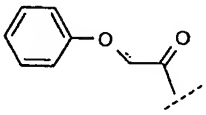
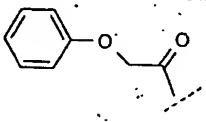
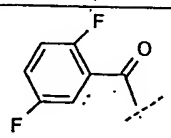
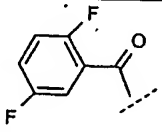
	LC - MS	R_a	R_b	R_c	Retention time (min)	
					B1a	B1b
Table A51	Z	CH_3		H	12.40	11.74
Table A52	Z	CH_3	$HCCCH_2NHC(O)$	H	12.22	11.53
Table A53	Z	CH_3	$(CH_3)_2NC(O)$	H	11.80	11.01
Table A54	Z	CH_3	$CH_3NHC(O)$	H	11.22	10.40
Table A55	Z	CH_3	$CH_3CH_2NC(O)$	H	12.11	11.38
Table A56	Z	CH_3	IPrNHC(S)	H	13.50	13.15
Table A57	Z	CH_3	$FCH_2C(O)$	H	12.08	11.37
Table A58	Z	CH_3	$F_2CHC(O)$	H	12.73	12.22
Table A59	W	CN	CH_3	H	9.27	8.59
Table A60	Z	CH_3	CH_3CO	CH_3	12.25	12.72
Table A61	Z	CH_3	$CH_3NHC(S)$	H	12.6	12.02
Table A62	Z	CH_3	$H_2NC(O)CH_2$	H	5.00	4.58
Table A63	Z	CH_3	$CH_3OC(O)CH_2$	H	6.19	5.68
Table A64	Z	CH_3	$CH_3CH_2OC(O)CH_2$	H	6.63	6.10
Table A65	Z	CH_3	$iPrOC(O)CH_2$	H	7.13	6.61
Table A66	Z	CH_3	$tBuOC(O)CH_2$	H	7.44	6.95
Table A67	Z	CH_3	$CH_3OCH_2C(O)$	CH_3	14.91	-
Table A68	Z	CH_3	$Me_2NOC(O)$	H	12.85	12.35
Table A69	Z	CH_3	CH_3NHSO_2	H	12.02	11.30
Table A70	Z	CH_3	CH_3SO_2	H	12.17	11.46
Table A71	Y	CH_3	tBuSO	H	9.34	8.76
Table A72	Z	CH_3	$(CH_3)_2CclS(O)$	H	13.33, 13.21	12.91, 12.77
Table A73	Z	HCC	H	H	5.04	4.59
Table A74	Z	HCC	$CH_3C(O)$	H	10.92	10.16

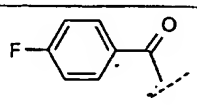
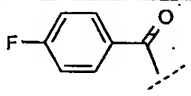
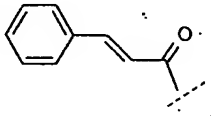
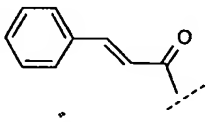
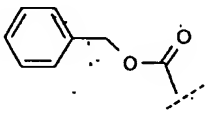
	LC-MS	R_a	R_b	R_c	Retention time (min)	
					B1a	B1b
Table A75	Z	HCC	$CH_3OCH_2C(O)$	H	11.89	11.16
Table A76	Z	HCC	$CH_3OC(O)$	H	12.10	11.41
Table A77	Z	$PhCH_2NC(O)$	$CF_3C(O)$	H	14.10	-
Table A78	Z	CH_3	$H_2NC(O)$	H	10.30	9.48
Table A79	Z	IPrNHC(O)	$CF_3C(O)$	H	13.98	13.72
Table A80	Z	tBuNHC(O)	$CF_3C(O)$	H	15.60	15.36
Table A81	Z	BuNHC(O)	$CF_3C(O)$	H	15.32	15.08
Table A82	Z	$CH_3O(CH_2)_2NHC(O)$	$CF_3C(O)$	H	14.63	-
Table A83	Z	$EtOC(O)CH_2NHC(O)$	$CF_3C(O)$	H	14.61	14.34
Table A84	Z	C6H11NHC(O)	$CF_3C(O)$	H	15.74	15.51
Table A85	Y	$Me_3SiCH_2NHC(O)$	$CF_3C(O)$	H	6.64	6.07
Table A86	Z	CH_3CC	H	H	11.12	10.48
Table A87	Y	CH_3OCH_2CC	H	H	7.37	7.02
Table A88	Y	CH_3	$-(CH_2)_4-$		3.67	3.47
Table A89	Y	CH_3OCH_2CC	$CH_3OCH_2C(O)$	H	8.51	7.90
Table A90	Y	CH_3	$BrCH_2(CH_2)_3OC(O)$	H	10.68	10.8
Table A91	Y	CH_3CC	$CH_3C(O)$	H	7.98	7.34
Table A92	Y	CH_3CC	$CH_3OCH_2C(O)$	H	8.80	8.21
Table A93	Y	CH_3OCH_2CC	$CH_3C(O)$	H	7.82	7.19
Table A94	Y	$BtCH_2NHC(O)$	$CF_3C(O)$	H	10.40	10.18
Table A95	Y	$tBuOC(O)N(CH_2)_2NHC(O)$	$CF_3C(O)$	H	10.77	-
Table A96	Y	$CH_3NHC(O)$	$CF_3C(O)$	H	9.88	9.41
Table A97	Y	$(CH_2)_2CHNHC(O)$	$CF_3C(O)$	H	10.52	10.11
Table A98	Y	$(CH_2)_4CHNHC(O)$	$CF_3C(O)$	H	11.68	11.31
Table A99	Y	EtNHC(O)	$CF_3C(O)$	H	10.48	-

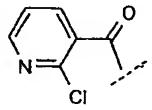
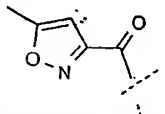
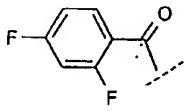
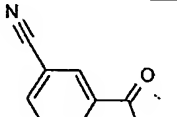
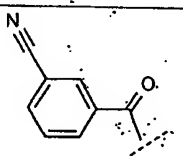
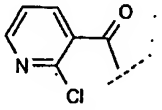
	LC - MS	R_a	R_b	R_c	Retention time (min)	
					B1a	B1b
Table A100	Y	$(CH_2)_2CHNHC(O)$	$CH_3C(O)$	H	9.02	8.42
Table A101	Y	iPrNHC(O)	H	H	3.64	3.44
Table A102	Y	iPrNHC(O)	$CH_3OCH_2C(O)$	H	9.42	8.91
Table A103	Y	BuNHC(O)	H	H	4.21	3.95
Table A104	Y	$CH_3O(CH_2)_2NHC(O)$	H	H	3.44	3.25
Table A105	Y	BuNHC(O)	$CH_3C(O)$	H	9.61	9.07
Table A106	Y	$CH_3O(CH_2)_2NHC(O)$	$CH_3C(O)$	H	7.77	-
Table A107	Y	CH_3	$(CH_2)_5$		3.69	3.49
Table A108	Y	CH_3	$Br(CH_2)_5OC(O)$	H	11.08	10.61
Table A109	Y	CH_3	$tBuSO_2$	H	10.01	9.45
Table A110	Y	$-CH_2$ NHC(O)		$CF_3C(O)$	12.85	12.53
Table A111	Y	$Me_3Si(CH_2)_2NHC(O)$	$CF_3C(O)$	H	12.33	11.99
Table A112	Y	$(CH_2)_2CHNHC(O)$	H	H	3.32	2.75
Table A113	Y	$(CH_2)_2CHNHC(O)$	$CH_3OCH_2C(O)$	H	8.91	8.35
Table A114	Y	$(CH_2)_2CHNHC(O)$	$CH_3C(O)$	H	8.38	7.77
Table A115	Y	iPrNHC(O)	HC(O)	H	8.86	8.26
Table A116	Y	CH_3	tBuOC(O)NH	H	9.86	9.31
Table A117	Y	$HOCH_2CH_2$	$CH_3C(O)$	H	3.40	-
Table A118	Y	CN	$BrCH_2C(O)$	H	9.23	-
Table A119	Y	HCC	PrC(O)	H	8.98	8.40
Table A120	Y	HCC	$Et_2CHC(O)$	H	10.03	9.52
Table A121	Y	HCC	iPrC(O)	H	9.01	8.45
Table A122	Y	HCC	EtC(O)	H	8.36	7.74
Table A123	Y	HCC	$(CH_2)_2CHC(O)$	H	8.80	8.22
Table A124	Y	HCC	$CH_3CHCHC(O)$	H	8.81	8.22

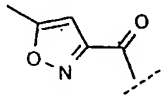
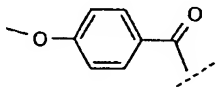
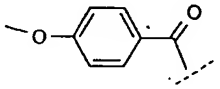
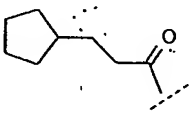
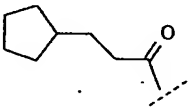
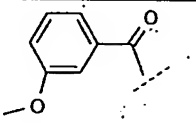
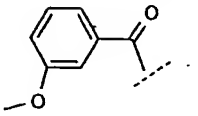
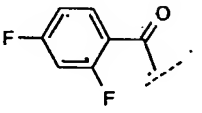
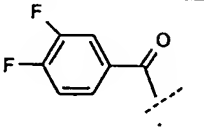
	LC - MS	R_a	R_b	R_c	Retention time (min)	
					B1a	B1b
Table A125	Y	HCC	$(CH_2)_3CHC(O)$	H	9.35	8.79
Table A126	Y	HCC	$CH_3CO_2C(CH_3)_2C(O)$	H	9.08	8.49
Table A127	Y	HCC	EtOC(O)	H	9.17	8.62
Table A128	Y	HCC	tBuC(O)	H	9.82	9.30
Table A129	Y	HCC	$iPrCH_2C(O)$	H	9.50	8.99
Table A130	Y	O_2NCH_2	H	H	4.11	3.84
Table A131	Y	O_2NCH_2	$CH_3C(O)$	H	8.67	8.08
Table A132	Y	O_2NCH_2	$CH_3OCH_2C(O)$	H	9.22	8.69
Table A133	Y	O_2NCH_2	$CH_3CHCHC(O)$	H	9.65	9.16
Table A134	Z	O_2NCH_2	EtC(O)	H	12.78	-
Table A135	Z	CH_3	EtNHC(S)	H	13.13	12.70
Table A136	W	CH_3	Propargyl	H	6.25	-
Table A137	Z	vinyl	$HC(O)OCH_2C(O)$	H	11.95	11.27
Table A138	Z	CH_3	$HC(O)OCH_2C(O)$	H	11.46	10.71
Table A139	Z	CN	$HC(O)OCH_2C(O)$	H	11.58	10.91
Table A140	Z	vinyl	$H_2NCH_2C(O)$	H	5.83	-
Table A141	Z	CH_3	$H_2NCH_2C(O)$	H	5.49	5.12
Table A142	Z	CN	$H_2NCH_2C(O)$	H	5.56	5.06
Table A143	Z	vinyl	$BrCH_2C(O)$	H	13.09	12.67
Table A144	Z	CH_3	$BrCH_2C(O)$	H	12.78	12.28
Table A145	A	CH_3	$CH_3O_2C(CH_2)_3C(O)$	H	1.7	-
Table A146	A	CH_3		H	-	2.0

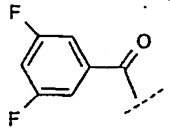
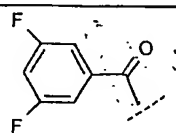
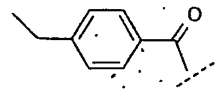
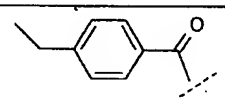
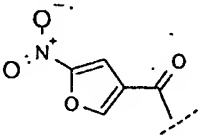
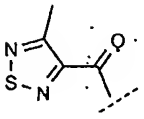
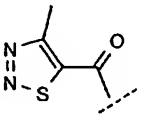
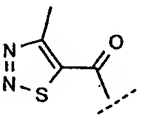
	LC - MS	R_a	R_b	R_c	Retention time (min)	
					B1a	B1b
Table A147	A	CH_3		H	2.2	-
Table A148	A	CH_3		H	-	1.8
Table A149	A	CH_3	$CH_3(CH_2)_5C(O)$	H	-	2.2
Table A150	A	CH_3	$CH_3(CH_2)_5C(O)$	H	2.3	-
Table A151	A	CH_3		H	-	2.1
Table A152	A	CH_3		H	2.2	-
Table A153	A	CH_3		H	-	2.1
Table A154	A	CH_3		H	2.2	-
Table A155	A	CH_3	$CH_3(CH_2)_6C(O)$	H	2.4	-
Table A156	A	CH_3		H	-	1.8
Table A157	A	CH_3		H	1.9	-
Table A158	A	CH_3	$CH_3(CH_2)_4C(O)$	H	2.1	-

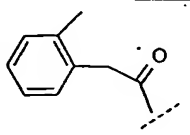
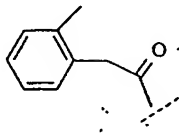
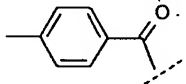
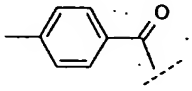
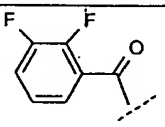
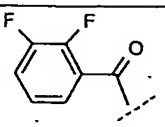
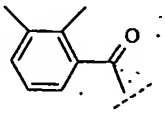
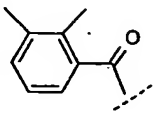
	LC - MS	R_a	R_b	R_c	Retention time (min)	
					B1a	B1b
Table A159	A	CH_3		H	-	1.87
Table A160	A	CH_3		H	2	-
Table A161	A	CH_3		H	-	1.96
Table A162	A	CH_3		H	2.1	-
Table A163	A	CH_3	$CH_2C(CH_3)OCH_2C(O)$	H	-	1.5
Table A164	A	CH_3	$CH_3(CH_2)_7C(O)$	H	2.6	-
Table A165	A	CH_3		H	-	2.0
Table A166	A	CH_3		H	2.2	-
Table A167	A	CH_3		H	-	2.0
Table A168	A	CH_3		H	2.2	-

	LC - MS	R_a	R_b	R_c	Retention time (min)	
					B1a	B1b
Table A169	A	CH_3		H	-	1.9
Table A170	A	CH_3		H	2.1	-
Table A171	A	CH_3	BuOC(O)	H	2.3	-
Table A172	A	CH_3	$ClCH_2CH_2OC(O)$	H	2.01	-
Table A173	A	CH_3	$CH_2C(CH_3)C(O)$	H	2.1	-
Table A174	A	CH_3		H	-	2.0
Table A175	A	CH_3		H	2.0	-
Table A176	A	CH_3	$H_2CCHCH_2CH_2OC(O)$	H	2.2	-
Table A177	A	CH_3		H	2.1	-
Table A178	A	CH_3	$(CH_2)_2CCHC(O)$	H	2.2	-
Table A179	Z	CH_2NO_2	PrC(O)	H	13.25	12.99
Table A180	Z	CH_3	OH	H	7.00	6.44
Table A181	A	CH_3	tBuC(O)	H	2.2	-
Table A182	A	CH_3	$(CH_3)_2CCHC(O)$	H	-	1.87
Table A183	A	CH_3	$Et_2CHC(O)$	H	2.2	-
Table A184	A	CH_3	$PhCH_2C(O)$	H	2.0	-
Table A185	A	CH_3	iPrC(O)	H	1.9	-
Table A186	A	CH_3	$IPrCH_2C(O)$	H	2	-

	LC - MS	R_a	R_b	R_c	Retention time (min)	
					B1a	B1b
Table A187	A	CH_3	EtC(O)	H	1.7	-
Table A188	A	CH_3	$(CH_2)_2CHC(O)$	H	1.8	-
Table A189	A	CH_3		H	1.89	-
Table A190	A	CH_3		H	-	1.9
Table A191	A	CH_3	$CH_3CHCHC(O)$	H	1.83	-
Table A192	A	CH_3	$(CH_2)_3CHC(O)$	H	2.0	-
Table A193	A	CH_3		H	-	2.05
Table A194	A	CH_3	$(CH_2)_4CHC(O)$	H	2.3	-
Table A195	A	CH_3	$CH_3CO_2C(CH_3)_2C(O)$	H	1.9	-
Table A196	A	CH_3		H	-	1.9
Table A197	A	CH_3		H	2	-
Table A198	A	CH_3	$ClCH_2(CH_2)_3OC(O)$	H	2.2	-
Table A199	A	CH_3		H	-	1.69

	LC - MS	R_a	R_b	R_c	Retention time (min)	
					B1a	B1b
Table A200	A	CH_3		H	2.1	-
Table A201	A	CH_3		H	-	1.9
Table A202	A	CH_3		H	2.1	-
Table A203	A	CH_3		H	-	2.2
Table A204	A	CH_3		H	2.3	-
Table A205	A	CH_3	$(CH_2)_5CHC(O)$	H	2.2	-
Table A206	A	CH_3		H	-	1.9
Table A207	A	CH_3		H	2.1	-
Table A208	A	CH_3		H	2.2	-
Table A209	A	CH_3		H	2.2	-

	LC - MS	R_a	R_b	R_c	Retention time (min)	
					B1a	B1b
Table A210	A	CH_3		H	-	2.1
Table A211	A	CH_3		H	2.2	-
Table A212	A	CH_3		H	-	2.17
Table A213	A	CH_3		H	2.3	-
Table A214	A	CH_3	$(CH_2)_4CHC(O)$	H	-	1.9
Table A215	A	CH_3		H	2.0	-
Table A216	A	CH_3		H	1.7	
Table A217	A	CH_3		H	-	1.8
Table A218	A	CH_3		H	1.9	-
Table A219	A	CH_3	$(CH_3)_2CH(CH_2)_2C(O)$	H	-	2.0
Table A220	A	CH_3	$(CH_3)_2CH(CH_2)_2C(O)$	H	2.2	-

	LC - MS	R_a	R_b	R_c	Retention time (min)	
					B1a	B1b
Table A221	A	CH_3		H	-	2
Table A222	A	CH_3		H	2.2	-
Table A223	A	CH_3		H	-	2
Table A224	A	CH_3		H	2.2	-
Table A225	A	CH_3	PrC(O)	H	-	1.7
Table A226	A	CH_3	$CH_3OC(O)(CH_2)_4C(O)$	H	1.8	-
Table A227	A	CH_3		H	-	2.01
Table A228	A	CH_3		H	2.2	-
Table A229	A	CH_3	$CH_3S(CH_2)_2C(O)$	H	1.9	-
Table A230	A	CH_3		H	-	2.1
Table A231	A	CH_3		H	2.3	-
Table A232	A	CH_3	$Et_2CHC(O)$	H	-	2.0

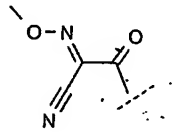
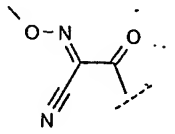
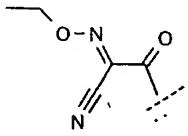
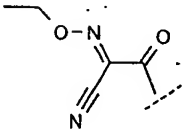
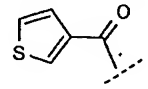
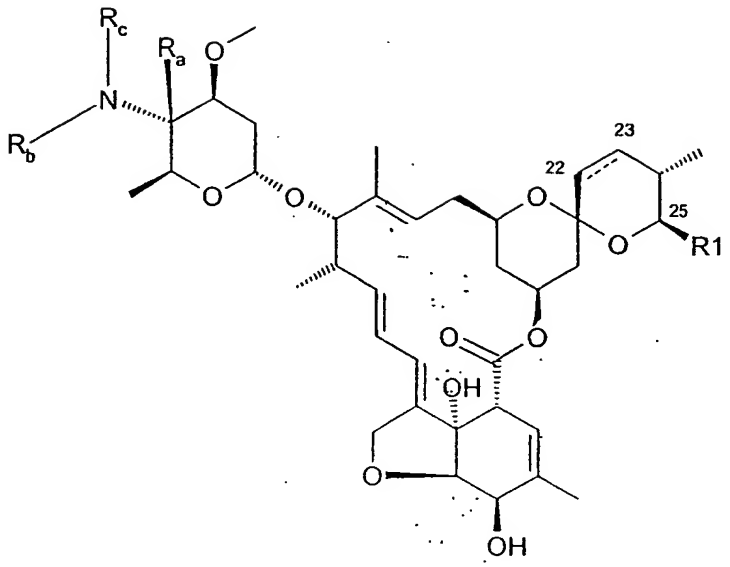
	LC - MS	R_a	R_b	R_c	Retention time (min)	
					B1a	B1b
Table A233	A	CH_3		H	-	1.9
Table A234	A	CH_3		H	2.0	-
Table A235	A	CH_3		H	-	2.0
Table A236	A	CH_3		H	2.2	-
Table A237	A	CH_3		H	2.0	-
Table A238	A	CH_3	$CH_3CH_2O_2C(CH_2)_3C(O)$	H	-	1.72
Table A239	A	CH_3	$CH_3CH_2O_2C(CH_2)_3C(O)$	H	1.9	-
Table A240	A	CH_3	$CH_3O_2C(CH_2)_3C(O)$	H	-	1.6

Table B: A compound of formula

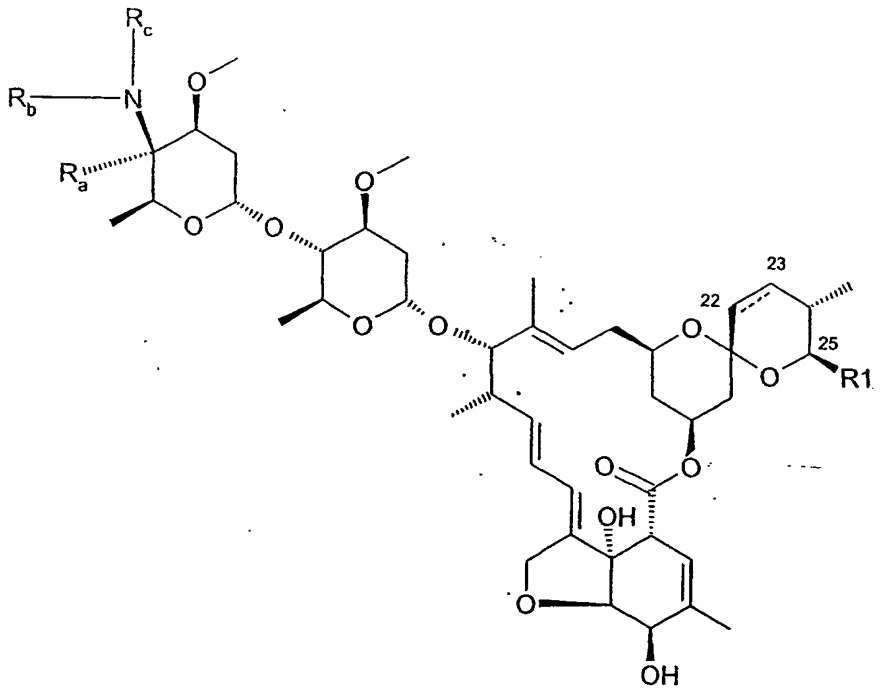


wherein R_1 is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

	LC-MS	R_a	R_b	R_c	Retention time (min)	
					B1a	B1b
Table B1	W	CH_3	H	H	4.71	4.46
Table B2	W	vinyl	H	H	4.94	4.71
Table B3	W	allyl	H	H	5.71	-
Table B4	W	vinyl	$CH_3OCH_2C(O)$	H	10.03	-
Table B5	W	vinyl	$CH_3C(O)$	H	8.85	8.00
Table B6	Z	vinyl	allyl	H	3.75	3.38
Table B7	Z	allyl	allyl	H	5.00	-
Table B8	Z	vinyl	Propargyl	H	5.70	5.06
Table B9	Z	Allyl	Propargyl	H	6.01	5.41
Table B10	Z	CN	CH_3	OH	10.34	9.63
Table B11	Z	O_2NCH_2	H	H	5.10	4.7
Table B12	Z	O_2NCH_2	$CH_3C(O)$	H	9.93	9.22
Table B13	Z	O_2NCH_2	PrC(O)	H	11.83	-

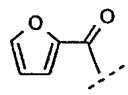
	LC-MS	R_a	R_b	R_c	Retention time (min)	
					B1a	B1b
Table B14	Z	O_2NCH_2	$CH_3OCH_2C(O)$	H	10.95	10.31
Table B15	Z	O_2NCH_2	iPrC(O)	H	11.94	11.28
Table B16	Z	O_2NCH_2	$CH_3OC(O)$	H	13.01	12.66
Table B17	Z	O_2NCH_2	$IPrCH_2C(O)$	H	12.46	11.98
Table B18	Z	O_2NCH_2	EtC(O)	H	10.97	10.30
Table B19	Z	O_2NCH_2	$(CH_2)_2CHC(O)$	H	11.41	10.75
Table B20	Z	O_2NCH_2	$CH_3CHCH\ C(O)$	H	11.55	10.87

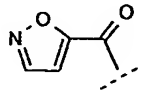
Table C: A compound of formula

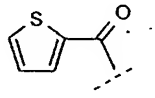


wherein R_1 is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond,and

	LC-MS	R_a	R_b	Rc	Retention time (min)	
					B1a	B1b
Table C1	W	CH_3	H	H	4.53	4.16
Table C2	W	vinyl	H	H	5.42	5.12
Table C3	W	Allyl	H	H	5.60	5.33
Table C4	W	$PhCH_2$	H	H	6.03	5.81
Table C5	W	HCC	H	H	5.32	5.07
Table C6	W	Ph	H	H	6.13	5.87
Table C7	W	CH_3	$CH_3C(O)$	H	9.82	9.01
Table C8	W	vinyl	$CH_3C(O)$	H	10.04	9.24
Table C9	W	Allyl	$CH_3C(O)$	H	10.24	-
Table C10	W	HCC	$CH_3C(O)$	H	9.13	-
Table C11	W	$PhCH_2$	$CH_3C(O)$	H	11.44	10.68
Table C12	X	$PhCH_2$	HC(O)	H	15.44	-
Table C13	W	CH_3	HC(O)	H	9.74	-
Table C14	W	vinyl	HC(O)	H	10.35	-
Table C15	W	Allyl	HC(O)	H	10.72	-
Table C16	W	HCC	HC(O)	H	9.43	-
Table C17	W	HCC	$CH_3OC(O)$	H	10.30	-
Table C18	W	CH_3	$CH_3CH_2OC(O)$	H	11.57	-
Table C19	W	HCC	$CH_3CH_2OC(O)$	H	10.94	-
Table C20	W	HCC	$CH_3OCH_2C(O)$	H	10.03	-
Table C21	Z	CH_3	$CH_3OCH_2CH_2C(O)$	H	11.28	-
Table C22	Z	CH_3	$CH_3CH_2OCH_2C(O)$	H	12.39	11.78
Table C23	W	CH_3	CH_3	CH_3	6.61	6.19
Table C24	W	HCC	CH_3	CH_3	5.87	5.65
Table C25	W	vinyl	allyl	H	6.08	5.76
Table C26	W	allyl	allyl	H	6.67	-

	LC-MS	R_a	R_b	Rc	Retention time (min)	
					B1a	B1b
Table C27	Y	CH_3	Propargyl	H	6.24	-
Table C28	W	Allyl	Propargyl	H	6.26	-
Table C29	W	CH_3	allyl	H	6.40	5.98
Table C30	Z	CH_3	CH_3	H	4.86	-
Table C31	Z	CH_3	CH_3	OH	5.78	-
Table C32	Z	CH_3	$OC(O)CH_3$	CH_3	12.95	12.50
Table C33	W	CN	H	H	8.25	7.62
Table C34	U	CN	$CH_3C(O)$	H	8.12	7.50
Table C35	W	CN	CH_3	H	8.76	8.6
Table C36	W	CN	$CH_3CH_2C(O)$	H	9.37	8.72
Table C37	W	CN	$CH_3OC(O)$	H	9.74	9.04
Table C38	W	CN	$(CH_2CH_2)CHC(O)$	H	9.65	8.96
Table C39	W	CN	$CH_3CH_2OC(O)$	H	9.60	9.02
Table C40	W	CN	$CH_3OCH_2C(O)$	H	10.01	9.28
Table C41	W	CN	$CH_2CHCH_2OC(O)$	H	10.52	9.87
Table C42	W	CN	tBuC(O)	H	11.25	10.59
Table C43	W	CN	$iPrCH_2$	H	10.48	9.79
Table C44	W	CN	$CH_3CH_2CH_2OC(O)$	H	10.99	10.37
Table C45	W	CN		H	10.56	9.87
Table C46	W	CN	$CH_2CHCH_2CH_2OC(O)$	H	10.98	10.38
Table C47	W	CN	$Et_2CHC(O)$	H	11.08	10.46
Table C48	W	CN	$CH_3(CH_2)_4C(O)$	H	10.95	10.34
Table C49	W	CN	$CH_3C(O)OCH_2C(O)$	H	9.14	8.47
Table C50	W	CN	$CH_3OC(O)CH_2C(O)$	H	9.67	9.02
Table C51	W	CN	$CH_3(CH_2)_3OC(O)$	H	11.48	10.88

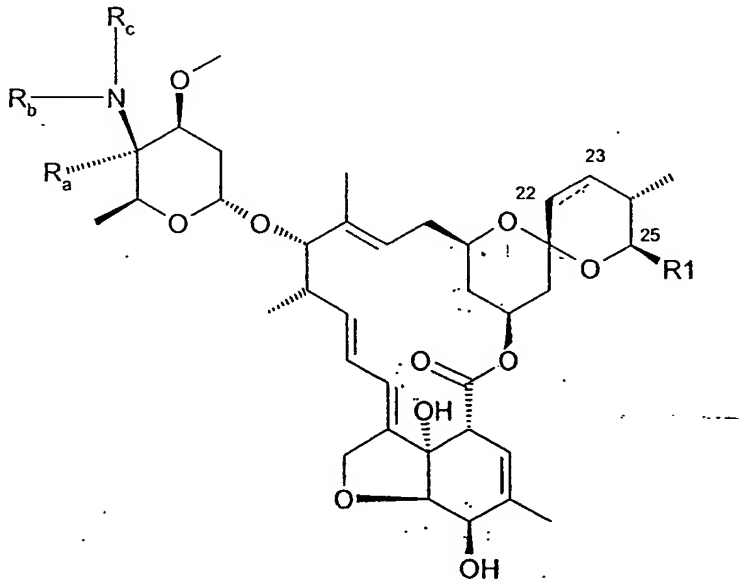
	LC-MS	R_a	R_b	Rc	Retention time (min)	
					B1a	B1b
Table C52	W	CN	$ClCH_2(CH_2)_2C(O)$	H	9.74	9.14
Table C53	W	CN	CyclohexylC(O)	H	11.31	10.68
Table C54	W	CN	$CH_3(CH_2)_5C(O)$	H	11.54	10.96
Table C55	W	CN	m-CH_3PhC(O)	H	11.19	10.58
Table C56	W	CN	$PhCH_2C(O)$	H	10.17	9.50
Table C57	W	CN	$ClCH_2C(CH_3)_2C(O)$	H	10.54	-
Table C58	W	CN	$ClCH_2(CH_2)_3C(O)$	H	9.30	-
Table C59	W	CN	p-FPhC(O)	H	10.77	10.15
Table C60	W	CN	m-FPhC(O)	H	10.72	10.07
Table C61	W	CN	o-FPhC(O)	H	11.27	10.64
Table C62	W	CN	$CH_3(CH_2)_6C(O)$	H	12.07	11.52
Table C63	W	CN	EtOC(O) $(CH_2)_2C(O)$	H	9.55	8.90
Table C64	W	CN	HC(O)	H	8.30	7.68
Table C65	W	CN	Bu	H	12.58	12.05
Table C66	W	CN	$tBuCH_2$	H	13.77	13.13
Table C67	W	CN	$(CH_2CH_2)CHCH_2$	H	12.59	12.00
Table C68	W	CN	$CH_3CH_2O(CH_2)_3$	H	12.11	-
Table C69	W	CN	$CH_3CH_2CH_2$	H	12.78	12.16
Table C70	W	CN	iPrC(O)	H	10.10	9.41
Table C71	W	CN	IPrOC(O)	H	10.63	-
Table C72	W	CN	$ClCH_2CH_2C(O)$	H	9.70	9.05
Table C73	W	CN		H	10.03	9.36
Table C74	W	CN	$tBuCH_2C(O)$	H	11.12	10.49
Table C75	W	CN	$Et_2NC(O)$	H	-	-

	LC-MS	R_a	R_b	Rc	Retention time (min)	
					B1a	B1b
Table C76	W	CN		H	10.73	-
Table C77	W	CN	o-CH_3PhC(O)	H	11.02	10.47
Table C78	W	CN	PhOC(O)	H	10.88	10.28
Table C79	Z	CH_3	FCH_2CO_2	CH_3	13.21	12.8
Table C80	Z	CH_3	$(CH_2)_2CHCO_2$	CH_3	13.51	13.18
Table C81	Z	CH_3	$EtCO_2$	CH_3	13.41	13.05
Table C82	Z	CH_3	$iPrCO_2$	CH_3	13.73	13.42
Table C83	Z	CH_3	$CH_3OCH_2CO_2$	CH_3	12.81	12.30
Table C84	Z	CH_3	$tBuCO_2$	CH_3	13.97	13.70
Table C85	Z	CH_3	$CH_3OC(O)CH_2CO_2$	CH_3	12.88	12.47
Table C86	Z	CH_3	Cl_2CHCO_2	CH_3	13.92	-
Table C87	Z	CN	FCH_2CO_2	CH_3	12.91	12.55
Table C88	Z	CN	$(CH_2)_2CHCO_2$	CH_3	13.28	12.96
Table C89	Z	CN	$iPrCO_2$	CH_3	13.51	13.23
Table C90	Z	CN	$CH_3OCH_2CO_2$	CH_3	12.69	12.27
Table C91	Z	CN	$tBuCO_2$	CH_3	13.73	13.49
Table C92	Z	CN	Cl_2CHCO_2	CH_3	13.68	13.44
Table C93	Z	CN	CH_3CO_2	CH_3	12.84	12.44
Table C94	Z	CN	CH_3OCO_2	CH_3	13.02	12.67
Table C95	Z	CN	$CH_3O_2CCH_2CO_2$	CH_3	12.78	12.04
Table C96	Z	CN	OH	CH_3	11.98	-
Table C97	Z	vinyl	CH_3CO_2	CH_3	13.23	12.86
Table C98	Z	vinyl	CH_3OCO_2	CH_3	13.32	12.96
Table C99	Z	vinyl	FCH_2CO_2	CH_3	13.40	13.09
Table C100	Z	vinyl	$(CH_2)_2CHCO_2$	CH_3	13.65	13.34

	LC-MS	R_a	R_b	Rc	Retention time (min)	
					B1a	B1b
Table C101	Z	vinyl	$iPrCO_2$	CH_3	13.87	13.58
Table C102	Z	vinyl	$tBuCO_2$	CH_3	14.12	13.86
Table C103	Z	vinyl	$(CH_2)_4CHCO_2$	CH_3	14.28	14.04
Table C104	Z	vinyl	$PhCO_2$	CH_3	14.13	13.87
Table C105	Z	vinyl	OH	CH_3	7.12	6.54
Table C106	Z	vinyl	Me_2NCO_2	CH_3	12.88	-
Table C107	Z	vinyl	OH	Allyl	12.02	11.35
Table C108	Z	CH_3	OH	Allyl	9.10	-
Table C109	Z	vinyl	OH	H	8.33	7.66
Table C110	Z	CH_3	OH	H	5.99	-
Table C111	Y	CH_3CC	$CH_3C(O)$	H	7.96	7.36
Table C112	Y	CH_3OCH_2 CC	$CH_3C(O)$	H	7.58	-
Table C113	Y	CH_3CC	$CH_3OCH_2C(O)$	H	8.81	8.21
Table C114	Y	CN	CH_3	H	9.16	8.63
Table C115	Y	O_2NCH_2	CH_3	H	3.59	3.36
Table C116	Y	CH_3	CH_3	Allyl	3.75	3.55
Table C117	Y	CH_3	CH_3	Allyl	3.70	3.50
Table C118	Y	CN	$BrCH_2C(O)$	H	9.04	8.51
Table C119	Y	O_2NCH_2	H	H	3.80	3.59
Table C120	Y	O_2NCH_2	$CH_3C(O)$	H	8.44	-
Table C121	Y	O_2NCH_2	$PrC(O)$	H	9.80	9.31
Table C122	Y	O_2NCH_2	$(CH_2)_2CHC(O)$	H	9.50	9.00
Table C123	Y	O_2NCH_2	$CH_3CHCHC(O)$	H	9.57	9.07
Table C124	Z	CN	$HC(O)CH_2C(O)$	H	11.31	10.65
Table C125	Z	CN	$H_2NCH_2C(O)$	H	5.18	-
Table C126	Z	CN	HC(O)	CH_3	10.53	9.89

	LC-MS	R_a	R_b	Rc	Retention time (min)	
					B1a	B1b
		22-23-dihydro				
Table C127	Z	CH_3	$CH_3OCH_2C(O)$	H	11.95	11.23
Table C128	Z	$-CH_2CH_2OSO_2-$		H	12.80	-
Table C129	Y	$-CH_2CH_2OC(Ph)$		-	6.50	-
Table C130	Z	CH_3	$CH_3OCH_2C(O)O$	H	14.20	13.78
Table C131	Z	CH_3	$CH_3C(O)O$	H	12.79	12.34
Table C132	W	CH_3	Allyl	H	6.03	5.66

Table D: A compound of formula



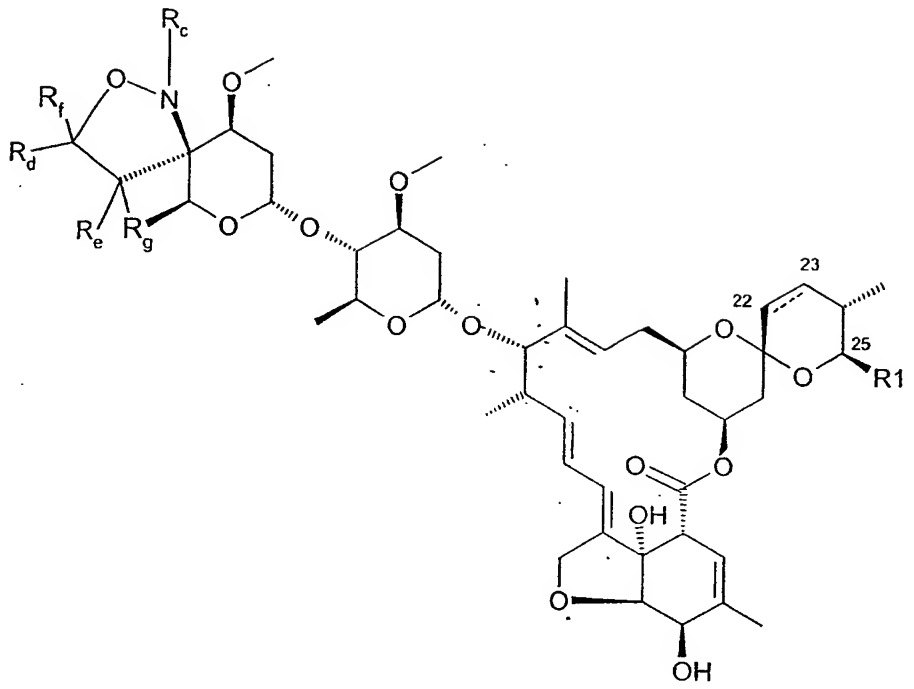
wherein R_1 is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

	LC-MS	R_a	R_b	R_c	Retention time (min)

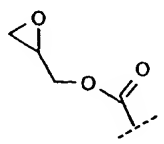
					B1a	B1b
Table D1	W	CH_3	H	H	3.95	-
Table D2	W	vinyl	H	H	4.06	-
Table D3	W	Allyl	H	H	5.71	-
Table D4	W	CH_3	$CH_3C(O)$	H	8.7	7.90
Table D5	W	CH_3	HC(O)	H	8.54	7.74
Table D6	W	vinyl	$CH_3C(O)$	H	7.04	-
Table D7	W	vinyl	$CH_3OCH_2C(O)$	H	8.31	-
Table D8	W	vinyl	$CH_3OC(O)$	H	8.64	-
Table D9	W	CH_3	$CH_3OCH_2C(O)$	H	9.56	8.70
Table D10	W	Allyl	$CH_3OC(O)$	H	9.43	8.71
Table D11	W	Allyl	$CH_3C(O)$	H	7.70	-
Table D12	Z	vinyl	allyl	H	3.75	-
Table D13	W	allyl	allyl	H	4.55	-
Table D14	Z	vinyl	Propargyl	H	6.19	-
Table D15	Z	Allyl	Propargyl	H	5.09	-
Table D16	W	CN	H	H	7.36	6.66
Table D17	W	CN	CH_3	H	8.39	8.05
Table D18	Z	CH_3	FCH_2CO_2	CH_3	12.24	11.69
Table D19	Z	CH_3	$(CH_2)_2CHCO_2$	CH_3	12.68	12.19
Table D20	Z	CH_3	$iPrCO_2$	CH_3	13.05	12.65
Table D21	Z	CH_3	$tBuCO_2$	CH_3	13.37	13.05
Table D22	Z	CH_3	$CH_3O_2CCH_2CO_2$	CH_3	11.71	11.07
Table D23	Z	CH_3	CH_3CO_2	CH_3	11.87	11.16
Table D24	Z	CH_3	CH_3OCO_2	CH_3	12.18	11.54
Table D25	Z	CH_3	$CH_3OCH_2CO_2$	CH_3	11.57	10.91
Table D26	Z	CH_3	Cl_2HCCO_2	CH_3	13.34	13.12
Table D27	Z	CN	CH_3CO_2	CH_3	11.57	10.91
Table D28	Z	CN	CH_3OCO_2	CH_3	11.92	11.31

	LC - MS	R_a	R_b	R_c	Retention time (min)	
					B1a	B1b
Table D29	Z	CN	$CH_3OCH_2CO_2$	CH_3	11.30	10.67
Table D30	Z	CN	FCH_2CO_2	CH_3	11.76	11.20
Table D31	Z	O_2NCH_2	H	H	4.94	4.53
Table D32	Z	O_2NCH_2	PrC(O)	H	12.13	11.55
Table D33	Z	O_2NCH_2	$(CH_2)_2CHC(O)$	H	11.86	11.22
Table D34	Z	O_2NCH_2	$CH_3CHCHC(O)$	H	11.91	11.28
Table D35	Z	O_2NCH_2	$CH_3C(O)$	H	10.65	9.86
Table D36	Z	O_2NCH_2	$IPrCH_2C(O)$	H	12.61	12.16
Table D37	Z	O_2NCH_2	EtC(O)	H	11.49	-
Table D38	Z	O_2NCH_2	$CH_3OCH_2C(O)$	H	11.41	-
Table D39	Z	O_2NCH_2	$CH_3OC(O)$	H	11.92	11.26
Table D40	Z	O_2NCH_2	iPrC(O)	H	12.20	11.63
Table D41	Z	O_2NCH_2	$Et_2CHC(O)$	H	13.03	12.65
Table D42	Z	O_2NCH_2	CH_3	H	4.70	4.30

Table E: A compound of formula

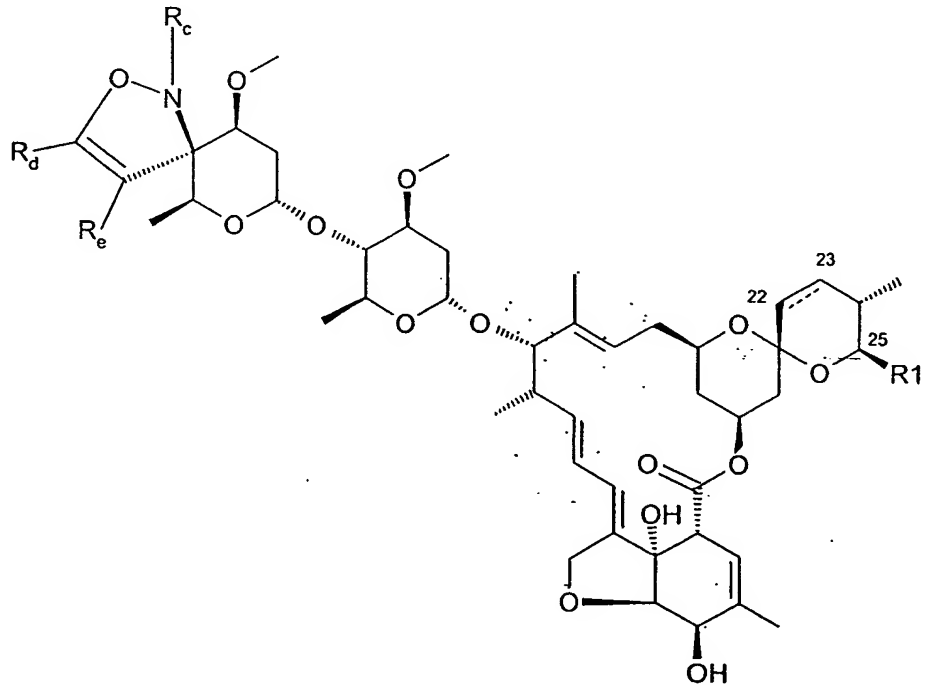


wherein R_1 is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

	LC-MS	R_c	R_d	R_e	R_f	R_g	Retention time (min)	
							B1a	B1b
Table E1	Z	CH_3	CO_2CH_3	H	H	H	14.78	-
Table E2	Z	CH_3	$CO_2CH_2CH_3$	H	H	H	12.75	-
Table E3	Z	CH_3		H	H	H	12.06	11.39
Table E4	Z	CH_3	CO_2tBu	H	H	H	13.39 13.49	13.06 13.17
Table E5	Z	CH_3	$PhSO_2$	H	H	H	13.27 13.17	- 12.80

	LC-MS	R_c	R_d	R_e	R_f	R_g	Retention time (min)	
							B1a	B1b
Table E6	Z	CH_3	OEt	H	H	H	12.32 11.80	- -
Table E7	Z	CH_3	$CH_2OC(O)CH_3$	H	H	H	11.67 11.19	- -
Table E8	Z	CH_3	CN	H	H	H	12.89 12.70	12.43 12.22
Table E9	Z	CH_3	o-FPh	H	H	H	13.51 -	13.22 -

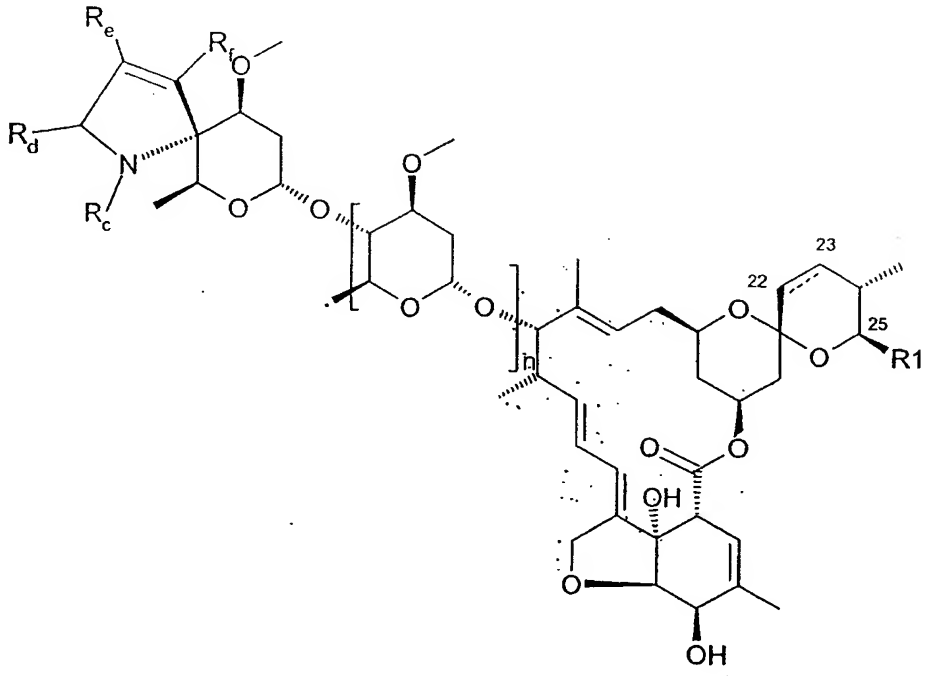
Table F: A compound of formula



wherein R_1 is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

	LC-MS	R_c	R_d	R_e	Retention time (min)	
					B1a	B1b
Table F1	Z	C(O)OMe	C(O)OMe	CH_3	13.34	13.02

Table G: A compound of formula

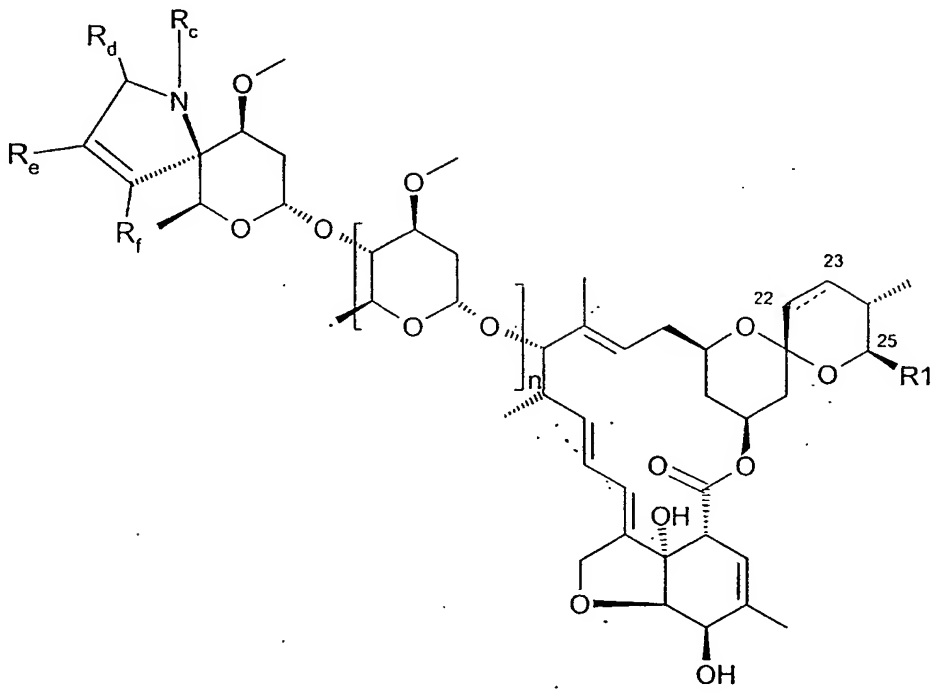


wherein R_1 is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

	LC-MS	n	R_c	R_d	R_e	R_f	Retention time (min)	
							B1a	B1b
Table G1	W	1	H	H	H	H	9.57	

Table G2	Z	0	H	H	H	H	3.94	-

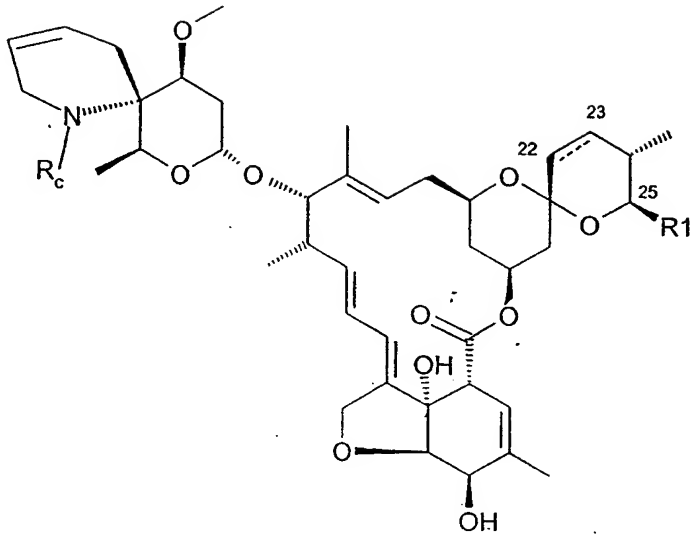
Table H: A compound of formula



wherein R_1 is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

		n	R_c	R_c	R_c	R_f	Retention time (min)	
	LC-MS						B1a	B1b
Table H1	W	1	H	H	H	H	9.87	-
Table H2	Z	0	H	H	H	H	3.47	-

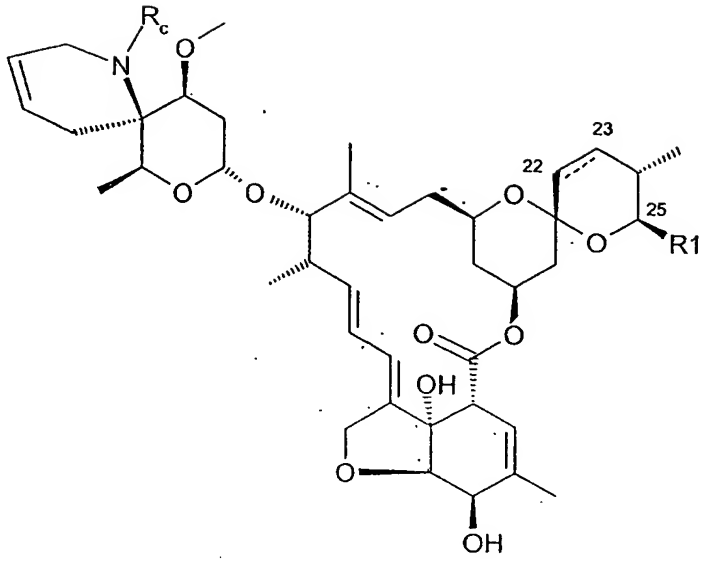
Table I: A compound of formula



wherein R_1 is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

		R_c	Retention time (min)	
			B1a	**B1b**
Table I1	Z	H	4.49	-

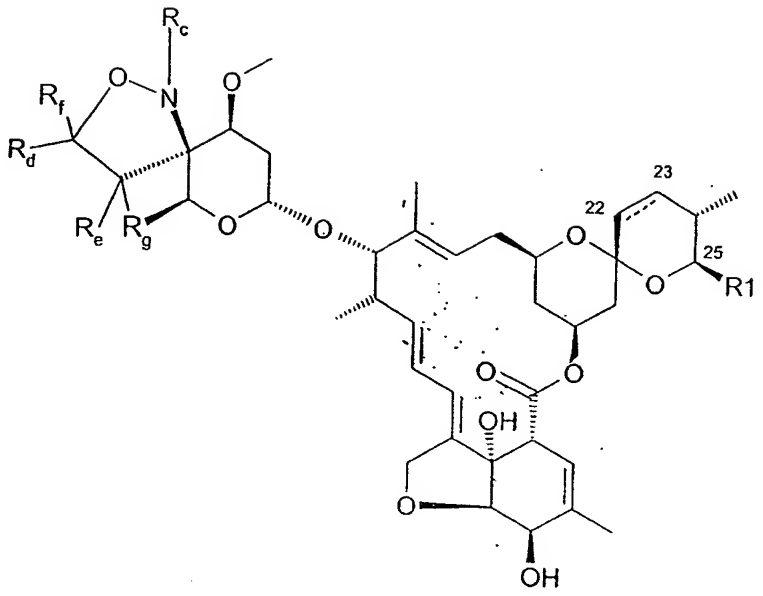
Table J: A compound of formula



wherein R_1 is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

		R_4	Retention time (min)	
			B1a	B1b
Table J1	Z	H	3.62-3.45	-

Table K: A compound of formula



wherein R_1 is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

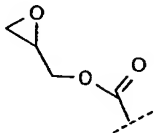
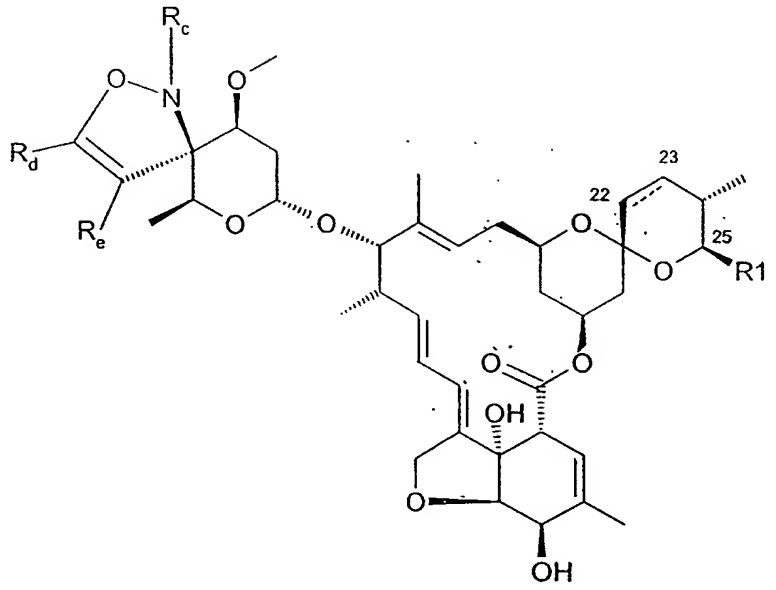
	LC-MS	R_c	R_d	R_e	R_f	R_g	Retention time (min)	
							B1a	B1b
Table K1	Z	CH_3	$CO_2CH_2CH_3$	H	H	H	11.16 11.46	10.39 -
Table K2	Z	CH_3		H	H	H	10.14 10.44	10.39 -
Table K3	Z	CH_3	CN	H	H	H	11.70 11.32	10.93 -
Table K4	Z	CH_3	OEt	H	H	H	10.82 9.88	- -
Table K5	Z	CH_3	$CH_2OC(O)CH_3$	H	H	H	9.75 9.29	- -

Table K6	Z	CH_3	o-FPh	H	H	H	12.77	12.27
Table K7	Z	CH_3	$PhSO_2$	H	H	H	12.20 12.34	11.49 11.75

Table L: A compound of formula



wherein R_1 is sec-butyl (B1a) or isopropyl (B1b) and the bond between carbon atoms 22 and 23 is a double bond, and

		R_c	R_d	R_e	Retention time (min)	
					B1a	**B1b**
Table L1	Z	C(O)OMe	C(O)OMe	CH_3	12.52	11.98

Also made available are compounds having the following characteristics:

Table M1	A compound corresponding to a line of Tables A to J, wherein R_1 is cyclohexyl.

Table M2	A compound corresponding to a line of Tables A to J, wherein R_1 is 1-methyl butyl.
Table M3	A compound corresponding to a line of Tables A to J, wherein the bond between the carbon atoms 22 and 23 is a single bond.
Table M4	A compound corresponding to a line of Tables A to J, wherein the configuration of the carbon atom at the ε position is opposite of that represented.
Table M5	A compound corresponding to a line of Tables A to J, wherein R_1 is cyclohexyl and the bond between the carbon atoms 22 and 23 is a single bond.
Table M6	A compound corresponding to a line of Tables A to J, wherein R_1 is 1-methyl butyl and the bond between the carbon atoms 22 and 23 is a single bond.
Table M7	A compound corresponding to a line of Tables A to J, wherein R_1 is cyclohexyl, the bond between the carbon atoms 22 and 23 is a single bond and the configuration of the carbon atom at the ε position is opposite of that represented.
Table M8	A compound corresponding to a line of Tables A to J, wherein R_1 is 1-methyl butyl, the bond between the carbon atoms 22 and 23 is a single bond and the configuration of the carbon atom at the ε position is opposite of that represented.

Biological Examples:

Example B1: Activity against Spodoptera littoralis

Young soya bean plants are sprayed with an aqueous emulsion spray liquor which comprises 12.5 ppm of active compound, and, after the spray coating has dried on, populated with 10 caterpillars of the first stage of Spodoptera littoralis and introduced into a plastic container. 3 days later, the reduction in the population in percent and the reduction in the feeding damage in per cent (% activity) are determined by comparing the number of dead caterpillars and the feeding damage between the treated and the untreated plants.

In this test, the compounds of formulae (I), (III), and (V) show good activity. In particular, the compound from Table A5, Table A6, Table A7, Table A8, Table A11, Table A13, Table A24, Table A42, Table B1, Table C1, Table C23, Table C29, Table D1, Table D2, Table D6, Table D8, Table D9, Table H1 effect a reduction in the pest population by more than 80%.

Example B2: Activity against Spodoptera littoralis, systemic:

Maize seedlings are placed into the test solution which comprises 12.5 ppm of active compound. After 6 days, the leaves are cut off, placed onto moist filter paper in a Petri dish and populated with 12 to 15 Spodoptera littoralis larvae of the L_1 stage. 4 days later, the reduction of the population in per cent (% activity) is determined by comparing the number of dead caterpillars between the treated and the untreated plants.

In this test, the compounds of formulae (I), (III), and (V) show good activity. In particular, the compound from Table A5, Table A6, Table A7, Table A8, Table A11, Table A13, Table A24, Table A42, Table B1, Table C1, Table C23, Table C29, Table D1, Table D2, Table D6, Table D8, Table D9, Table H1 effect a reduction in the pest population by more than 80%.

Example B3: Activity against Heliothis virescens

35 0- to 24-hour-old eggs of Heliothis virescens are placed onto filter paper in a Petri dish on a layer of synthetic feed. 0.8 ml of the test solution which comprises 12.5 ppm of active compound, is then pipetted onto the filter papers. Evaluation is carried out after 6 days. The reduction in the population in per cent (% activity) is determined by comparing the number of dead eggs and larvae on the treated and the untreated filter papers.

In this test, the compounds of formulae (I), (III), and (V) show good activity. In particular, the compound from Table A5, Table A6, Table A7, Table A8, Table A11, Table A13, Table A24, Table A42, Table B1, Table C1, Table C23, Table C29, Table D1, Table D2, Table D6, Table D8, Table D9, Table H1 effect a reduction in the pest population by more than 80%.

Example B4: Activity against Plutella xylostella caterpillars

Young cabbage plants are sprayed with an aqueous emulsion spray liquor which comprises 12.5 ppm of the active compound. After the spray coating has dried on, the cabbage plants are populated with 10 caterpillars of the first stage of Plutella xylostella and introduced into a plastic container. Evaluation is carried out after 3 days. The reduction in the population in per cent and the reduction in the feeding damage in per cent (% activity) are determined by

comparing the number of dead caterpillars and the feeding damage on the treated and the untreated plants.

In this test, the compounds of formulae (I), (III) and (V) show good activity against Plutella xylostella. In particular, the compound from Table A5, Table A6, Table A7, Table A8, Table A11, Table A13, Table A24, Table A42, Table B1, Table C1, Table C23, Table C29, Table D1, Table D2, Table D6, Table D8, Table D9, Table H1 effect a reduction in the pest population by more than 80%.

Example B5: Activity against Frankliniella occidentalis

In Petri dishes, discs of the leaves of beans are placed onto agar and sprayed with test solution which comprises 12.5 ppm of active compound, in a spraying chamber. The leaves are then populated with a mixed population of Frankliniella occidentalis. Evaluation is carried out after 10 days. The reduction in per cent (% activity) is determined by comparing the population on the treated leaves with that of the untreated leaves.

In this test, the compounds of formulae (I), (III), and (V) show good activity. In particular, the compound from Table A5, Table A6, Table A7, Table A8, Table A11, Table A13, Table A24, Table A42, Table B1, Table C1, Table C23, Table C29, Table D1, Table D2, Table D6, Table D8, Table D9, Table H1 effect a reduction in the pest population by more than 80%.

Example B6: Activity against Diabrotica balteata

Maize seedlings are sprayed with an aqueous emulsion spray liquor which comprises 12.5 ppm of active compound and, after the spray coating has dried on, populated with 10 larvae of the second stage of Diabrotica balteata and then introduced into a plastic container. After 6 days, the reduction in the population in per cent (% activity) is determined by comparing the dead larvae between the treated and the untreated plants.

In this test, compounds of formula (I), (III), and (V) show good activity, in particular, the compound from Table A8, Table A9, Table A11, Table A12, Table C23.

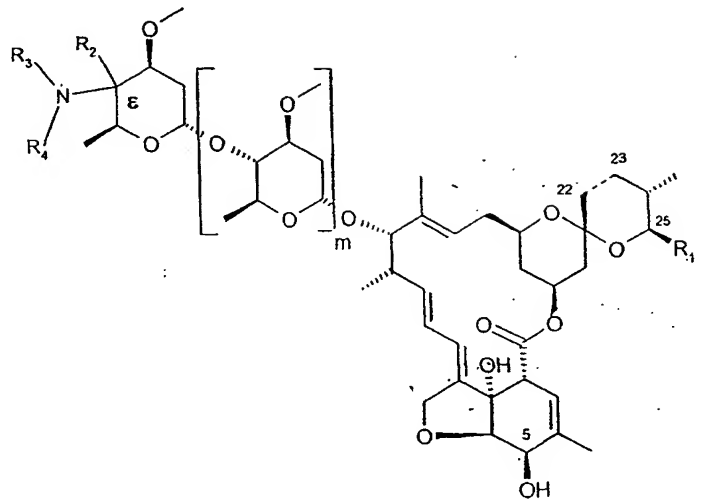
Example B7: Activity against Tetranychus urticae

Young bean plants are populated with a mixed population of Tetranychus urticae and, after 1 day, sprayed with an aqueous emulsion spray-liquor which comprises 12.5 ppm of active compound, incubated at 25°C for 6 days and then evaluated. The reduction in the population in per cent (% activity) is determined by comparing the number of dead eggs, larvae and adults on the treated and on the untreated plants.

In this test, the compounds of formulae (I), (III), and (V) show good activity. In particular, the compound from Table A5, Table A6, Table A7, Table A8, Table A11, Table A13, Table A24, Table A42, Table B1, Table C1, Table C23, Table C29, Table D1, Table D2, Table D6, Table D8, Table D9, Table H1 effect a reduction in the pest population by more than 80%.

CLAIMS

1. A compound of the formula (I)



(I),

wherein the bond between carbon atoms 22 and 23 indicated with a broken line is a single or double bond,

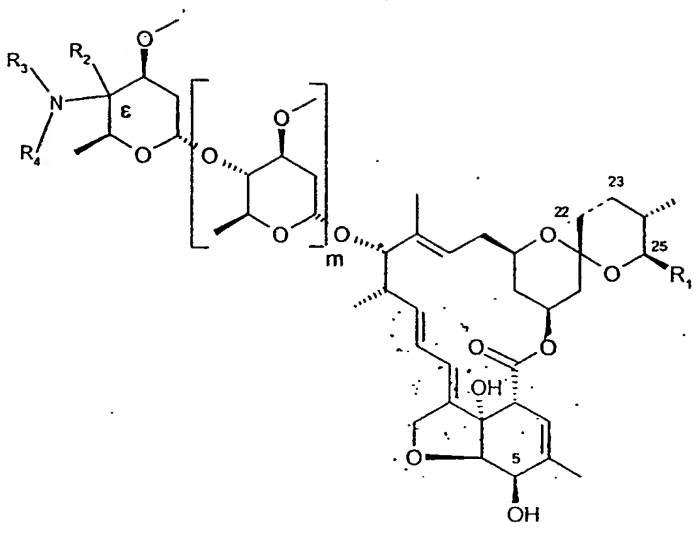
m is 0 or 1,

R_1 represents a C_1-C_{12}alkyl, C_3-C_8cycloalkyl or C_2-C_{12}alkenyl group,

R_2 represents a hydrocarbyl group or a substituted hydrocarbyl group, and

R_3 and R_4 represent, independently of each other, hydrogen or a chemical constituent, or either R_2 and R_3 together or R_3 and R_4 together represent a three- to seven-membered alkylene or a four- to seven-membered alkenylene bridge, for each of which at least one, preferably a CH_2 group may be replaced by O, S or NR_6, where R_6 represents hydrogen or a hydrocarbyl group or a substituted hydrocarbyl group; or, if appropriate, an E/Z isomer and/or tautomer of the compound of formula (I), in each case in free form or in salt form.

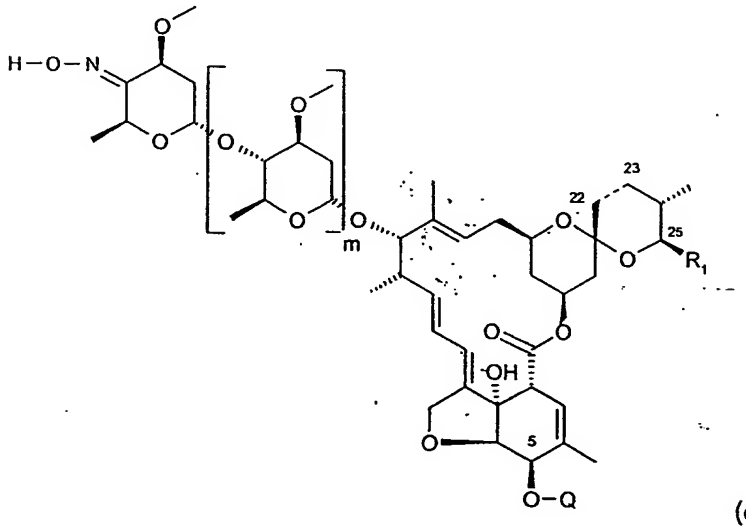
2. A process for preparing a compound of formula (I)



(I)

wherein R_1, R_2, R_3, R_4, the bond between the carbon atoms 22 and 23 and m are as defined in claim 1, comprising the steps of:

(i) synthesizing a compound of formula (α)



(α)

wherein R_1, the bond between the carbon atoms 22 and 23 and m are as defined for formula (I) in claim 1 and Q is a protecting group;

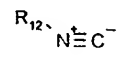
(ii) reacting a disulfide, an aliphatic or aromatic phosphine and a compound of formula (α) to yield a sulfenimine derivative of the compound of formula (α);

(iii) oxidising the sulfenimine derivative of the compound of formula (α) to yield a sulfinimine derivative of the compound of formula (α);

either

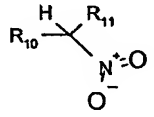
(iva) reacting an organometallic reagent having the R_2 group with the sulfinimine derivative of the compound of formula (α) to yield a desoxy –'sulfinamide - hydrocarbyl derivative of the compound of formula (α); or

(ivb) reacting an isocyanate reagent of formula



where R_{12} is unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkenyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkynyl, unsubstituted or mono- to pentasubstituted aryl, unsubstituted or mono- to pentasubstituted benzyl unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl ester, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl ester, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl sulfone or unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl nitrile with the sulfinimine derivative of the compound of formula (α) to yield a desoxy – amine - hydrocarbyl derivative of the compound of formula (α); or

(ivc) reacting an nitro alkyl reagent of formula



where R_{10} and R_{11} are independently of each other, H, CN, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkenyl, unsubstituted or mono- to

pentasubstituted C_2-C_{12}alkynyl, unsubstituted or mono- to pentasubstituted aryl, unsubstituted or mono- to pentasubstituted benzyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl ester, an unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl ester, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl sulfone or unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl nitrile with the sulfinimine derivative of the compound of formula (α) to yield a desoxy – amine - hydrocarbyl derivative of the compound of formula (α); and

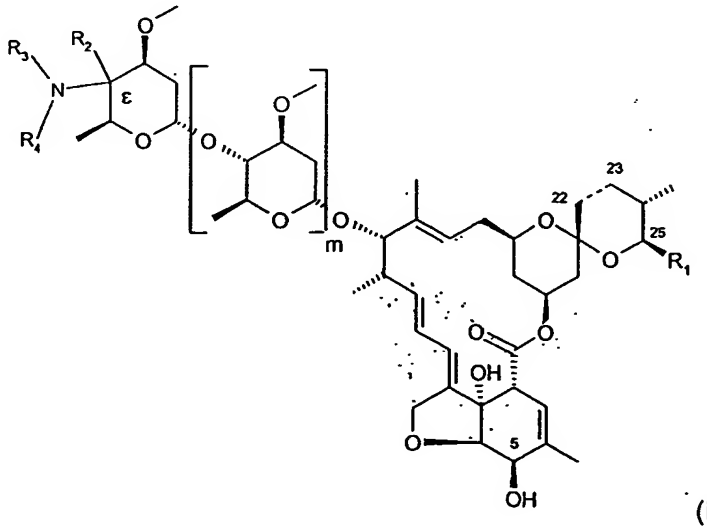
either

(va) removing the sulfinyl group and protecting group Q either in one step or sequentially one after another to yield a compound of formula (I), where R_3 and R_4 each represent hydrogen, or

(vb) removing the sulfinyl group alone, carrying out reactions on one or more of the R_2, R_3 and R_4 groups to modify the group and then removing the protecting group Q to yield a compound of formula (I), or

(vc) removing the protecting group Q if the sulfinyl group is removed during (iva) or (ivb) or (ivc) to yield a compound of formula (I).

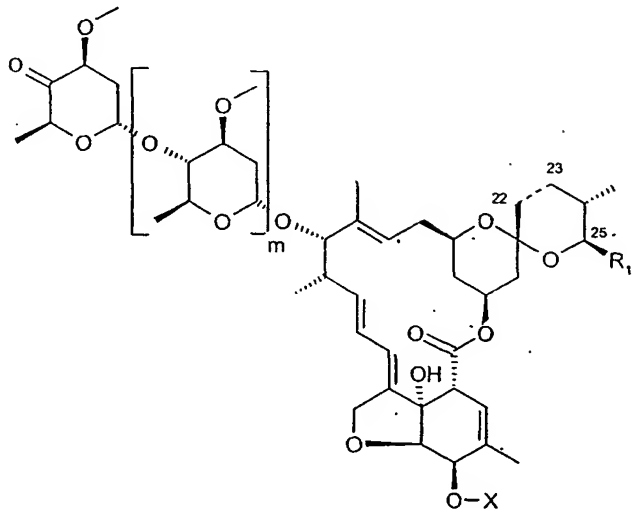
3. A process for preparing a compound of formula (I)



(I)

wherein R_1, R_2, R_3, R_4, the bond between the carbon atoms 22 and 23 and m are as defined in claim 1, comprising the steps of:

(i) synthesizing a compound of formula (β)



(β)

wherein R_1, the bond between the carbon atoms 22 and 23 and m is as defined for formula (I) in claim 1 and X is H or Q, where Q is a protecting group;

(ii) reacting N-R_4hydroxylamine or salt thereof with a compound of formula (β) to yield a nitrone derivative of the compound of formula (β);

either

(iiia) reacting an organometallic or a silyl reagent having the R_2 group with nitrone derivative of the compound of formula (β) to yield a desoxy – N-R_4hydroxylamino - hydrocarbyl

derivative of the compound of formula (β), where R_4 is as defined for formula (I) in claim 1, or

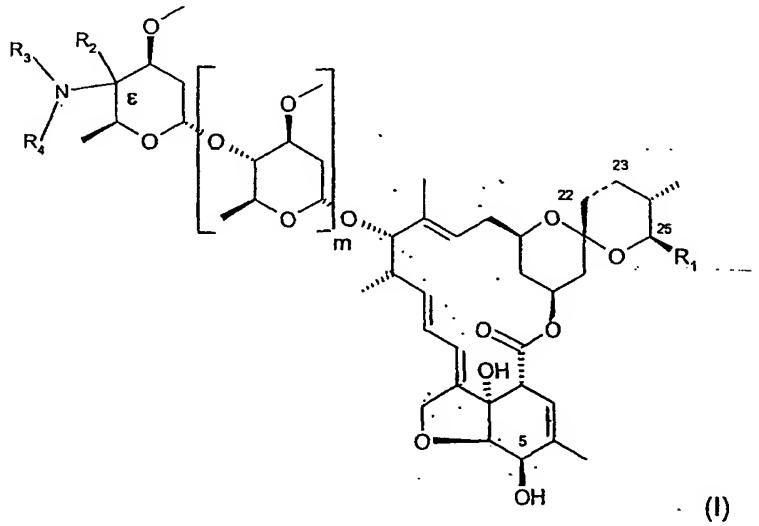
(iiib) reacting an alkene or an alkyne derivative with the nitrone derivative of the compound of formula (β) to yield a desoxy – N-isoxazolidine derivative or 2,3-dihydro-isoxazole derivative respectively of the compound of formula (β); and

either

(iva) removing the protecting group Q, if present, to yield a compound of formula (I), where R_3 is OH in the event of reaction step (iiia), or where R_2 and R_3 is an alkylene or alkenylene bridge with a CH_2 group replaced by an oxygen atom in the event of reaction step (iiib), or

(ivb) carrying out reactions on one or more of R_2, R_3 and R_4 groups to modify the group and removing the protecting group Q, if present, to yield a compound of formula (I).

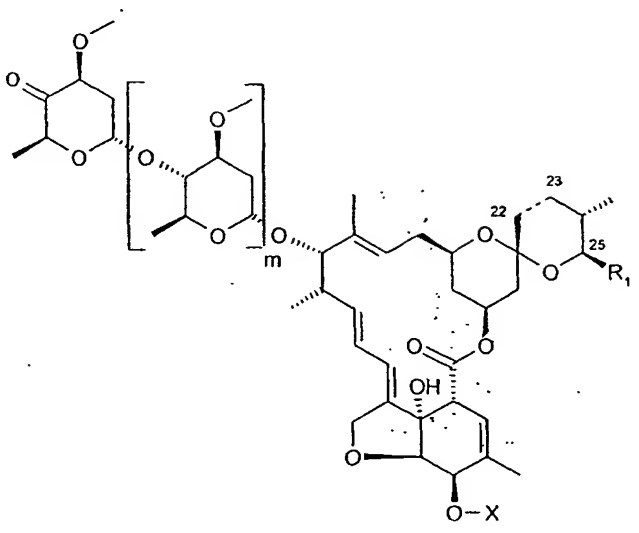
4. A process for preparing a compound of formula (I)



(I)

wherein R_1, R_3, R_4, the bond between the carbon atoms 22 and 23 and m are as defined in claim 1 and R_2 is CN, comprising the steps of:

(i) synthesizing a compound of formula (β)



(β)

wherein R_1, the bond between the carbon atoms 22 and 23 and m is as defined in for formula (I) in claim 1 and X is H or Q, where Q is a protecting group;

either

(iia) reacting the compound of formula (β) with a silylated amine (having the R_3 and R_4 groups) in presence of a Lewis acid and a trialkylsilyl cyanide, to yield a compound of formula (I) with the proviso that the oxygen atom at the 5-carbon position is protected, if Q is present, and wherein R_1, R_3, R_4, the bond between the carbon atoms 22 and 23 and m are as defined in claim 1, and R_2 is CN, or

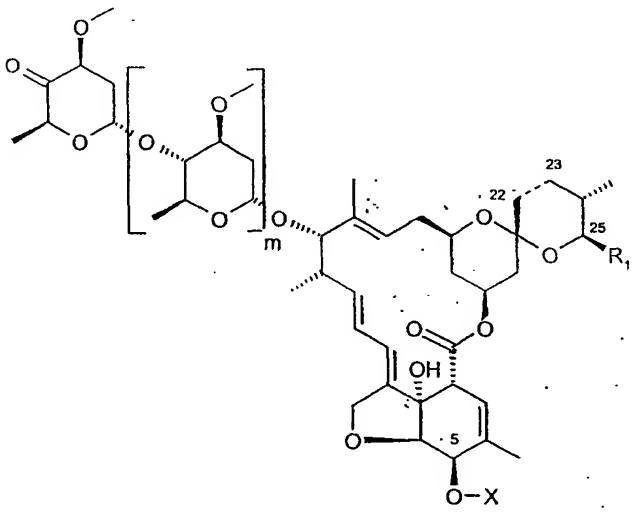
(iib) reacting the compound of formula (β) with an amine of formula R_3R_4NH, a chlorosilane, a Lewis acid and a trialkylsilyl cyanide to yield a compound of formula (I) with the proviso that the oxygen atom at the 5-carbon position is protected, if Q is present, and wherein R_1, R_3, R_4, the bond between the carbon atoms 22 and 23 and m are as defined in claim 1, and R_2 is CN;

(iii) optionally carrying out reactions on one or both of R_3 and R_4 groups to modify the group; and

(iv) removing the protecting group Q, if present, to yield a compound of formula (I);

or

(i) synthesizing a compound of formula (β)



(β)

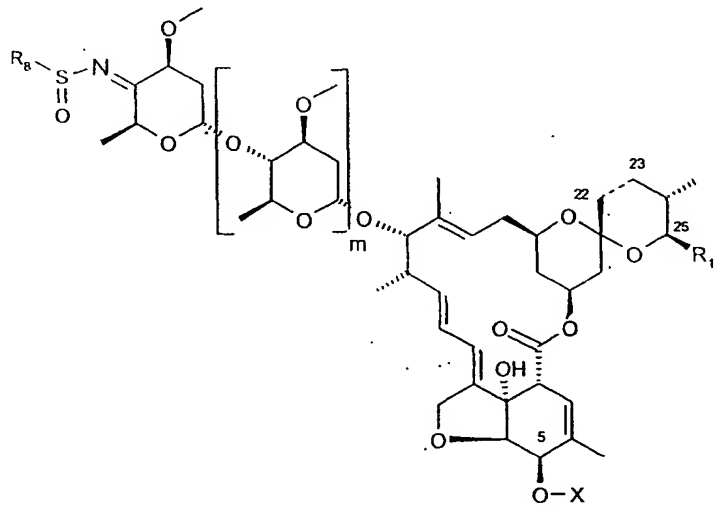
wherein R_1, the bond between the carbon atoms 22 and 23 and m are as defined for formula (I) in claim 1 and X is H or Q, where Q is a protecting group;

(ii) reacting the compound of formula (β) with an ammonium salt of formula $R_{18}CO_2^-NH_4^+$, an isocyanide of formula $R_{12}NC$ to yield a compound of formula (I), with the proviso that the oxygen atom at the 5-carbon position is protected, if Q is present in the compound of formula (β), wherein R_1, the bond between the carbon atoms 22 and 23 and m are as defined in claim 1, R_2 is $R_{12}NHC(O)$, and R_4 is $R_{18}C(O)$, R_{18} is H, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl, unsubstituted or mono- to pentasubstituted C_3-C_{12}cycloalkyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkenyl, unsubstituted or mono- to pentasubstituted C_2-C_{12}alkynyl, unsubstituted or mono- to pentasubstituted aryl, unsubstituted or mono- to pentasubstituted benzyl, unsubstituted or mono- to

pentasubstituted C_3-C_{12}cycloalkyl ester, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl ester, unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl sulfone or unsubstituted or mono- to pentasubstituted C_1-C_{12}alkyl nitrile and R_{12} is as defined in claim 2; and

(iii) removing the protecting group Q, if present, to yield a compound of formula (I).

5. A compound of the formula (III)



(III)

wherein the bond between carbon atoms 22 and 23 indicated with a broken line is a single or double bond,

m is 0 or 1,

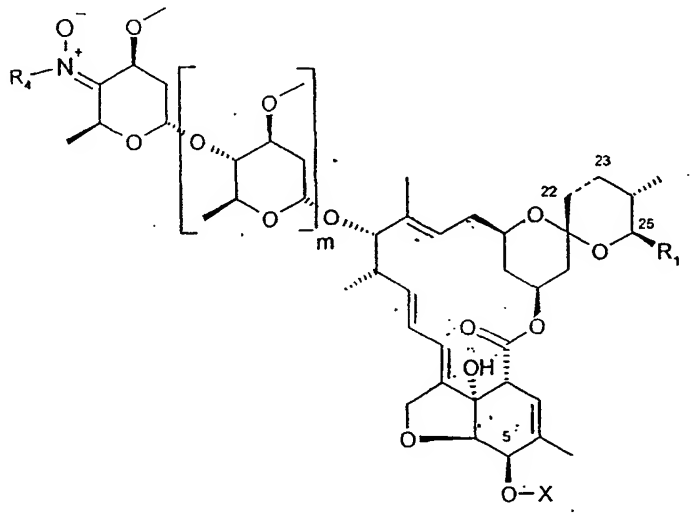
R_1 represents a C_1-C_{12}alkyl, C_3-C_8cycloalkyl or C_2-C_{12}alkenyl, group,

R_8 represents C_1-C_6alkyl that is optionally substituted with one to five substituents selected from the group consisting of halogen, C_1-C_6alkoxy, hydroxy, cyano, aryl, benzyl or heteroaryl, which, depending on the possibilities of substitution on the ring, are mono- to trisubstituted by substituents selected from the group consisting of OH, halogen, CN, NO_2, C_1-C_{12}alkyl, C_1-C_{12}haloalkyl, C_1-C_{12}alkoxy, C_1-C_{12}haloalkoxy, C_1-C_{12}alkylthio and C_1-C_{12}haloalkylthio, and

X represents H or Q, where Q is a suitable protecting group to prevent reaction on the oxygen atom at the 5-carbon position;

or, if appropriate, an E/Z isomer and/or diastereoisomer and/or tautomer of the compound of formula (III), in each case in free form or in salt form.

6. A compound of the formula (V)



(V)

wherein the bond between carbon atoms 22 and 23 indicated with a broken line is a single or double bond,

m is 0 or 1,

R_1 represents a C_1-C_{12}alkyl, C_3-C_8cycloalkyl or C_2-C_{12}alkenyl, group,

R_4 represents a chemical constituent, and

X represents H or Q, where Q is a suitable protecting group to prevent reaction on the oxygen atom at the 5-carbon position; or, if appropriate, an E/Z isomer and/or diastereoisomer and/or tautomer of the compound of formula (V), in each case in free form or in salt form.

7. A pesticidal composition comprising at least one compound of the formula (I), (III) or (V), as defined in claim 1, 5 or 6 respectively, as active compound, and at least one auxiliary.

8. A method for controlling pests comprising applying a composition defined claim 7 to the pests or their habitat.

9. A process for preparing a composition defined in claim 7 comprising mixing intimately and/ or grinding at least one compound least one compound of the formula (I), (III) or (V), as defined in claim1, 5 or 6 respectively, as active compound, with at least one auxiliary.

10. The use of a compound of the formula (I), (III) or (V), as defined in claim 1, 5 or 6 respectively, for preparing a composition as defined in claim 7.

11. The use of a composition as defined in claim 7 for controlling pests.

12. A method for protecting plant propagation material comprising treating the propagation material, or the location where the propagation material is planted, with a composition defined in claim 7.

13. A pest resistant plant propagation material having adhered thereto at least one compound of the formula (I), (III) or (V), as defined in claim 1, 5 or 6 respectively; preferably treated by the method of claim 12.

14. The use of compound defined in claim 5 or 6 for preparing a compound of formula (I) as defined in claim 1.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2005/002489

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07H19/01 A01N43/90 A61K31/7048 A61P33/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07H A01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 375 393 A (MERCK & CO. INC) 27 June 1990 (1990-06-27)	
A	WO 93/15099 A (PFIZER LIMITED; PFIZER INC) 5 August 1993 (1993-08-05)	
A	EP 0 343 708 A (MERCK & CO. INC) 29 November 1989 (1989-11-29) cited in the application	

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 June 2005	01/07/2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Bardili, W

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